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CONSTRUCTION OF A NEW ESOPHAGUS BY MEANS OF THE TRANSVERSE COLON AND ITS APPLICATION FOR CAUSTIC ATRESIA, CARCINOMA, AND VARICES OF THE ESOPHAGUS

REPORT OF 26 CASES

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SUBSTITUTION of the esophagus by the colon was first performed almost 50 years ago. The original reports of Vulliet[6] and Kelling[1] in 1911 in which these authors mentioned the performance of an esophagoplasty by means of the colon caused considerable comment. Many surgical procedures using different segments of the colon for this purpose have been tried since then. In all of them the colon was placed in a prethoracic or retrosternal position. The intrathoracic and transpleural route for the colon was recently proposed by Orsoni and Lemaire,[5] who did not apply it in any clinical case, however.

In 1952 we[4] reported the first case of esophagoplasty by means of the transverse colon placed in an intrathoracic and intrapleural position. The operation was performed on a young girl who had atresia of the esophagus caused by the ingestion of caustic soda and had been feeding herself through a gastrostomy for about 4 years. The final result of this operation was considered very successful. Since that time we have had the opportunity to perform this operation in 13 additional cases of atresia caused by the ingestion of caustic soda, in 10 cases of cancer, and in 2 varices of the esophagus. Our full experience with the esophagoplasty by means of the transverse colon in an intrathoracic and intrapleural position consists of 26 cases. The report of these cases is the subject of this paper.

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All patients were referred to us by the Service of Endoscopy of the Hospital das Clinicas, under the care of Dr. Plinio de Mattos Barreto.

METHOD

Separate descriptions of the techniques used for surgical treatment of atresia and of cancer and varices will be presented due to the different problems arising in these diseases.

Caustic Atresia.—It is difficult to plan a uniform technique of operation in this clinical entity, due to the variability of the extension of lesions produced by the caustic, which usually affects only the thoracic esophagus, but sometimes also the cervical esophagus or the stomach or both.

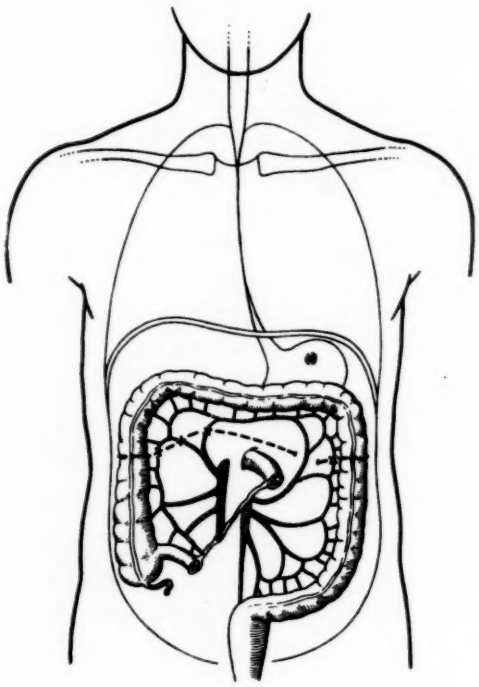

Fig. 1.

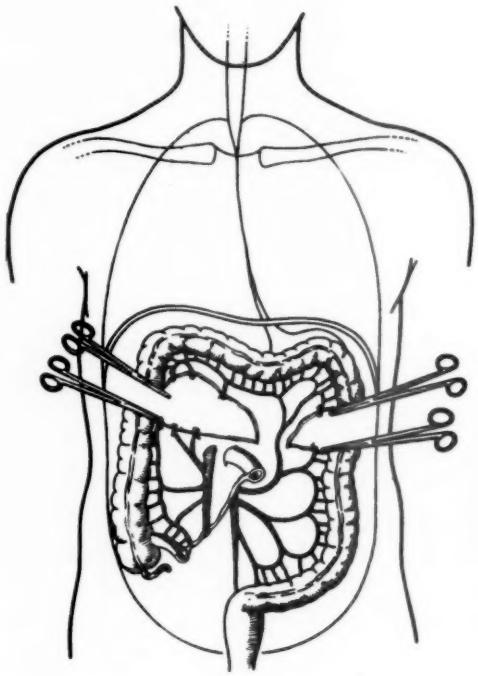

Fig. 2.

Fig. 1.—Levels of the vascular ligatures and of the colic sections.
Fig. 2.—Segment of the colon to be used in the esophagoplasty. Blood supply guaranteed by the left colic artery.

Abdominal Stage.—The abdomen is opened through a right-sided Lennander's incision. The large omentum is dissected free from the transverse colon and the hepatic and the splenic flexures are freed from their attachments. The blood supply of the colon is studied chiefly concerning the main vessels and the Drummond arcade. Ligature of the right and the medial colic vessels as well as the marginal arcade at the proposed levels of the colic section is performed (Fig. 1). Nutrition of the transverse colon to be used for the esophagoplasty is thus guaranteed only by the left colic vessels. Ascending and descending colons are cut close to the hepatic and splenic flexures, respectively (Fig. 2), and re-establishment of the intestinal continuity is made by means of an end-to-end anastomosis between the ascending and the descending colons, with two rows of interrupted cotton sutures. An opening is made then in the gastrohepatic omentum, through which the isolated loop of colon is passed. This maneuver avoids

the compression by the great gastric curvature of the mesentery harboring the left colonic vessels. The excluded transverse colon is placed in the left subphrenic region and the abdominal wall is closed.

Thoracoabdominocervical Stage.—While the abdominal wall is being closed, a left cervicotomy is performed medially to the sternocleidomastoid muscle down to the pleural cupola by another team of surgeons. The esophagus is exposed, dissected, and divided. If the distal stump is fibrotic and completely obliterated, as usually occurs, no special care is needed; if, however, persistence of the lumen is noted, it is necessary to close it by suture with interrupted cotton, sutures. The cervical wound is temporarily protected with a dressing and the thoracic stage of the operation is started after turning the patient upon his right side. Left thoracotomy is performed through the eighth intercostal space. It is sometimes necessary to resect the eighth rib. The diaphragm is opened and the excluded transverse colon is brought up to the pleural cavity. An opening is made then in the pleural cupola by means of combined cervical and intrapleural digital maneuvers. The proximal stump of the colon is exteriorized up to the cervical wound through this opening after placing the colon in the paravertebral gutter behind the lung. Anastomosis of the distal stump of the colon to the gastric fundus is made then with two rows of interrupted cotton sutures. The diaphragmatic opening is closed, not too tight around the colon, in order to avoid compression of its mesentery. The thoracic wound is closed after passing a drainage tube through the tenth intercostal space.

The patient is returned to the supine position and anastomosis between the esophagus and the colon is performed with two rows of interrupted cotton sutures (Fig. 3). The cervical wound is closed and the operation is finished (Fig. 4).

When the lesion affects the cervical esophagus as well as the thoracic esophagus, the anastomosis of the colon is made with the hypopharynx instead of the cervical esophagus (Fig. 5). When the lesion involves the stomach, also causing a retraction and fibrosis of the organ, the anastomosis of the colon is made with a jejunal loop instead of the stomach. When a previous subtotal gastrectomy has been carried out, the anastomosis of the colon is made with the efferent jejunal loop of the gastrojejunal anastomosis.

When the patient's general condition and especially the local conditions of the cervical esophagus are not favorable for the primary esophagocolic anastomosis, it is desirable to postpone it to another stage after these conditions have been overcome by a proper treatment.

Cancer and Varices.—When the general condition of the patient is satisfactory, total esophagectomy and esophagocoloplasty may be carried out in a single stage. In the majority of the cases, however, the patient's condition does not allow the performance of such a formidable procedure; the operation is best performed in two stages. In the first one the total thoracic esophagectomy is done through a right thoracotomy; the cardia is closed and the cervical esophagus is brought out through a left cervical stab wound. A gastrostomy is constructed to feed the patient temporarily (Fig. 6). In the second stage, which is carried out 2 or 3 months later, after the general condition of the patient has

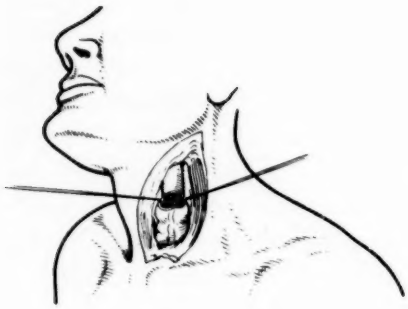

Fig. 3.

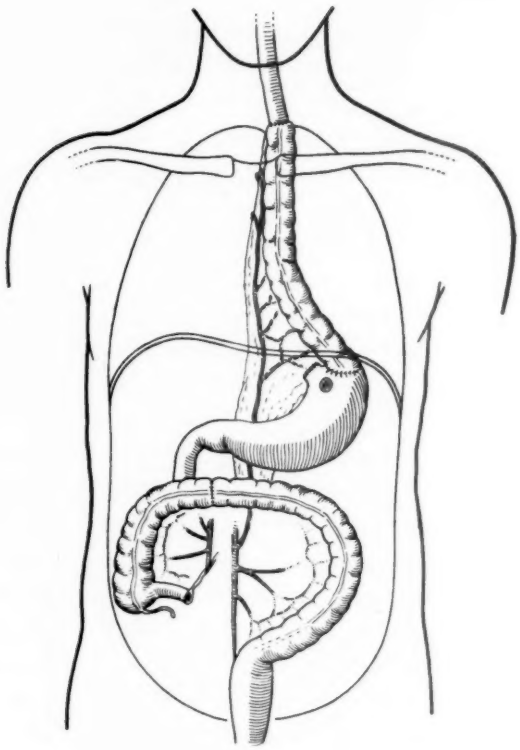

Fig. 4.

Fig. 3.—Anastomosis between the cervical esophagus and the colon.
Fig. 4.—Final aspect of the operation. Esophagocolic and gastrocolic anastomosis.

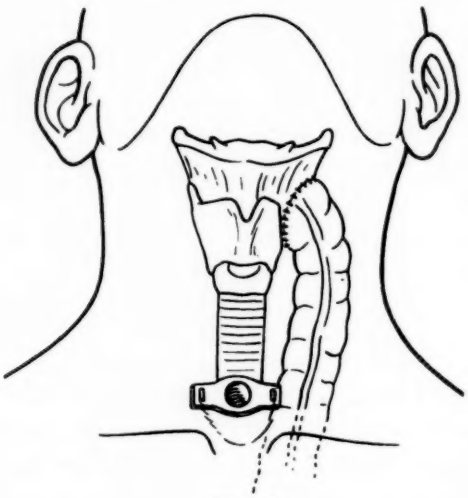

Fig. 5.

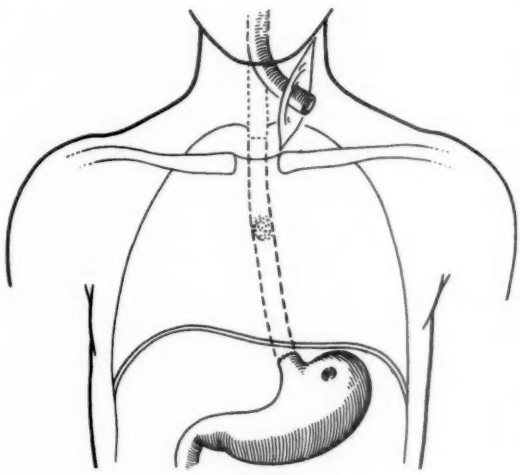

Fig. 6.

Fig. 5.—Anastomosis between the hypopharynx and the colon.
Fig. 6.—Total thoracic esophagectomy for cancer. Cervical esophagus brought out through a left cervical stab wound. Distal stump of the esophagus closed at the level of the cardia. Gastrostomy for temporary feeding of the patient.

improved, the esophagocoloplasty is performed according to the technique described for caustic atresia. In some cases, due to the very bad general condition of the patient, a gastrostomy prior to the performance of the esophagectomy is recommended.

It must be pointed out that the gastrostomy closes spontaneously in almost every case as soon as the patient starts to feed himself through the new esophagus. Only occasionally surgical closure becomes necessary.

PERSONAL EXPERIENCE

As previously mentioned, 26 patients were submitted to the esophagocoloplasty. Indications for this operation are given in Table I.

TABLE I

	NUMBER OF CASES
Caustic atresia	14
Cancer	10
Varices	2
Total	26

Caustic Atresia.—All the patients with caustic atresia were young people. Ages ranged between 7 and 32 years. Eleven were women and 3 men. In all but the youngest, atresia resulted from ingestion of caustic soda as an attempt to commit suicide. In every case of this series re-establishment of esophageal continuity had previously been attempted by Hurst bougie. In 5 cases Freitas-Mattos Barretto's operation[2] for recanalization of the esophagus had also been performed. Only after failure of these treatments was the esophagocoloplasty indicated.

In 9 patients the operation was performed in two stages. In the first one the esophagocoloplasty was carried out, but no attempt was made to perform the esophagocolic anastomosis. The proximal stump of the colon was left in the neck as a colostomy. In the second stage, the operation was completed by the performance of such anastomosis. In 5 patients the operation was performed in one stage. The main reason for the performance of the operation in two stages was the fear that, if esophagocolic fistula would occur, anterior mediastinitis would result due to the lack of adequate adhesive protection of the anastomotic region. After observing that when fistula develops no mediastinitis results and also after more experience with the operation, preference has been given to the performance of the esophagocoloplasty in one stage. The convalescence has been smoother and the economic advantages are obvious.

In 3 cases the anastomosis of the proximal stump of the colon was made with the hypopharynx because the cervical esophagus was also involved in the cicatricial process. In 2 cases the anastomosis of the distal stump of the colon was made with the jejunal loop, because the caustic corrosion also attacked the stomach, which became fibrotic, retracted and therefore improper for suturing. In one patient, who had been previously submitted to a subtotal gastrectomy, the anastomosis of the colon was made with the efferent jejunal loop of the gastrojejunal anastomosis.

In the first patient of our series, the anastomosis of the colon was made with the proximal jejunal loop instead of the stomach because of fear of a corrosive ulcer formation in the mucosa of the colon by the gastric juice. However such a concept soon changed after it was demonstrated by one of us[3] in experimental work on dogs that ulcer formation does not occur when anastomosis of the colon is made in the fundus of the stomach. It must be recalled that this was also the only patient in whom the esophagocoloplasty was constructed in an antiperistaltic position.

Cancer.—All the cancer patients were over 40 years of age. The youngest was 43 and the oldest was 60 years old. All were men. The dysphagia had a duration of 3 weeks to one year. The average duration of this symptom was 5 months. The cancer was located in the proximal third of the organ in 2 cases, in the middle third in 7 cases, and in the distal third in one case. The histopathologic studies showed squamous-cell carcinoma in 8 cases, spindle-cell tumor in one case, and solid carcinoma in another case.

A total thoracic esophagectomy was previously performed through a right thoracotomy in all of these cases. The esophagocoloplasty was performed from one to 3 months later. In 8 cases this operation was performed in one stage and in 2 in two stages; in both of these cases the esophagocoloplasty was completed by the performance of the esophagocolic anastomosis one month later.

Varices.—The two cases with varices were men 24 and 29 years of age, respectively. In both cases varices resulted from schistosomotic portal hypertension and were bleeding seriously. They were submitted first to a total thoracic esophagectomy and later to the esophagocoloplasty, in two stages.

RESULTS

There were 5 postoperative deaths in our series of cases, as is shown in Table II.

TABLE II. MORTALITY

	NUMBER OF CASES	DEATHS	PER CENT
Caustic atresia	14	2	14.3
Cancer	10	2	20.0
Varices	2	1	50.0
Total	26	5	19.2

In 2 cases death was due to peritonitis, caused by leakage at the colocolic anastomosis. In one the operation was performed for cancer and in the other for varices. In one case death resulted from anoxemia consequent to an immediate postoperative hypertensive pneumothorax. The esophagocoloplasty was performed for cancer. In another one death resulted form anoxemia, consequent to an immediate postoperative edema of the trachea; the patient had mild stenosis of this organ caused by the caustic soda. In the last one death resulted probably from an anterior mediastinitis. The operation was performed for atresia caused by caustic soda.

The main postoperative complications, besides those which resulted in death, were injury to the left recurrent nerve and esophagocolic fistula formation. The former occurred in 3 patients, 2 in cases of atresia and one of cancer. They were

followed by paralysis of the correspondent vocal cord, but no serious consequences resulted. Esophagocolic fistula occurred in 6 patients, 4 of whom were operated upon for atresia and 2 for cancer. In all of them it was mild in character and healed spontaneously in 2 or 3 weeks. In no case was a complementary operation necessary.

All the patients started to swallow after the operation without any difficulty, expect the 3 in whom anastomosis of the colon was made to the hypopharynx; however, with proper re-education they also were able later to swallow fairly well. Swallowing was also normal as soon as healing occurred in those patients in whom esophagocolic fistula developed.

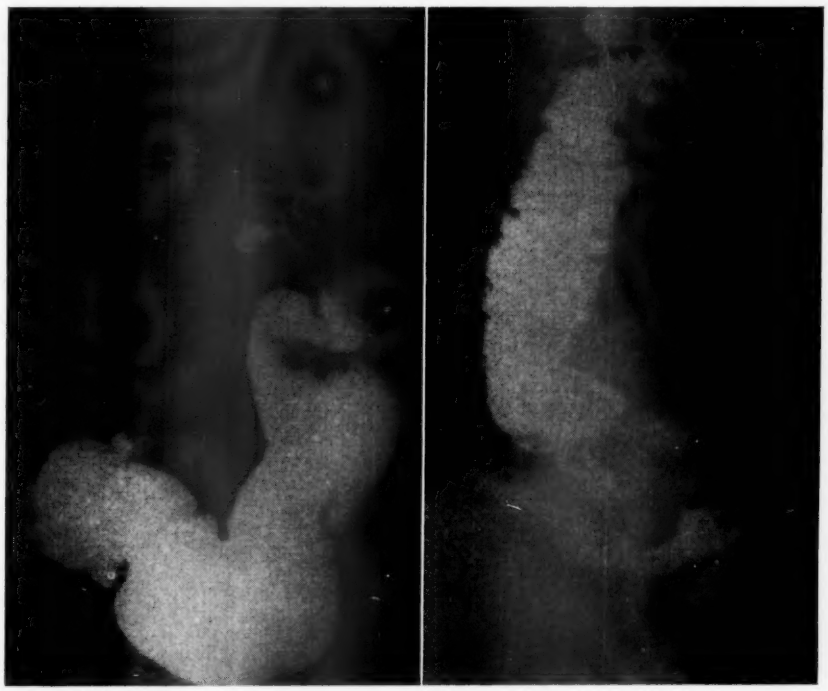

Fig. 7. Fig. 8.

Fig. 7.—X-ray taken 6 months after the performance of the esophagocoloplasty. Note the good emptying of the colon and barium in the stomach.

Fig. 8.—X-ray taken one month after the performance of the esophagocoloplasty. Anastomosis of the colon was made with the jejunum because the stomach was fibrotic and retracted. Note barium in the colon and in the jejunal loop.

There was slight regurgitation through the new esophagus in 3 patients as they assumed the recumbent position. This trouble subsided spontaneously in some weeks, without any special care. No patient complained of fecaloid odor.

Control radiologic studies were undertaken on most of the patients. As it was expected, passage of the barium meal through the new esophagus was slower than normally. It took about 1 to 2 minutes for the head of the contrast meal to reach the stomach or the jejunum. In all cases the new esophagus retained the morphologic character of the colon, with its typical haustra (Figs. 7 and 8). However in one case "esophagization" of the colon was observed one year after the operation (Fig. 9). Although the contrast meal proceeded slowly in all patients examined, no stasis was observed.

Improvement of the general condition was noted in all cases of atresia. All patients gained weight, sometimes as much as 35 pounds in one year. They were extremely happy with their new condition. The sensation of drinking and eating again by mouth after feeding themselves through gastrostomies for several years was extremely impressive, both for the patients and the surgeons.

The follow-up studies of the cancer cases showed that of the 8 patients who survived the operation, 3 died of metastasis 11, 14 and 15 months after the operation, respectively. Of the remaining 5 patients, one was alive for almost 4 years, another for 9 months after the resection, and 3 were not followed.

The patient with varices who survived the operation feels very well after 15 months have elapsed since the performance of the operation. No further bleeding has occurred.

Fig. 9.

Fig. 10.

Fig. 9.—"Esophagization" of the colon one year after the performance of the esophagocoloplasty. No haustra observed.

Fig. 10.—Colon prepared for the esophagocoloplasty. Note the viability of the loop, the blood supply of which is guaranteed by the left colic artery. It measured almost 2 feet.

DISCUSSION

The use of the transverse colon has been a very valuable method of substitution for the esophagus. Several reasons justify the use of this intestinal loop for this purpose: (1) it is a long segment, sometimes as much as 2 feet, which makes its transposition up to the cervical region very easy (Fig. 10); (2) its nutrition, guaranteed by the left colic artery, is very adequate; and (3) the technique of its exclusion does not offer any difficulty.

In performing the esophagocoloplasty some special technical problems must be considered. In the esophagocologastric anastomosis it is better to put the colon in the isoperistaltic position, since it reduces considerably the possibility of gastric juice regurgitation. It was used in all but the first case of our series. The regurgitation is also lessened by the performance of the anastomosis of the colon to the fundus instead of the middle part of the stomach. It must be pointed out, however, that when this trouble occurs it has the tendency to subside spontaneously in some weeks. In no case of our series was colic peptic ulcer formation noted.

In caustic atresia of the esophagus, no attempt must be made to remove this organ. Besides being reduced to a thin rigid tube, its presence does not cause any trouble to the patient.

Our present conduct in the surgical treatment of cancer of the esophagus is the performance of a total thoracic esophagectomy and re-establishment of the esophagogastric transit by means of the esophagocoloplasty. We believe that in performing the total thoracic esophagectomy there is a better chance of cure, because the possibility of leaving residual cancer infiltration of the wall, as sometimes is observed when partial resection is performed, is avoided. In carrying out this wide resection one has the problem of re-establishment of the transit between the cervical esophagus and the stomach. This can be done by means of a gastroesophageal anastomosis in the neck, which is technically difficult and gives rise to a terrible reflux esophagitis; or by means of an esophagojejunal anastomosis, which often results in breakdown of a part of the jejunal wall due to difficulty in obtaining and keeping a good blood supply to the long jejunal segment needed for such an anastomosis; or finally by means of an esophagocoloplasty which proves to be much better according to our experience. The performance of the esophagocoloplasty 2 or 3 months after the esophagectomy, as we have done in our cases, also gives a chance to the patient to improve his general condition and therefore to stand this formidable surgical procedure better. We are not yet able to affirm that our concept in handling this disease is the best one, since we have not followed a sufficient number of patients long enough. We have the impression, however, that more satisfactory results are obtained with this procedure.

The esophagectomy followed by esophagocoloplasty is not to be performed as a routine method in portal hypertension varices of the esophagus. It seems to us, however, that it has a place in those cases in which other surgical methods of treatment have failed, chiefly the "shunt" operations. Our experience is very small and does not allow us to estimate the real value of the concept we are proposing.

SUMMARY

Our experience with 26 cases of esophagocoloplasty by means of the transverse colon is reported. The originality of the operation is that the colon is placed in an intrathoracic and intrapleural position. The operation was performed on 14 patients with atresia caused by the ingestion of caustic soda, on 10 patients with cancer and on 2 with varices of the esophagus.

Details of the technique of the esophagocoloplasty are described separately for each of these clinical entities and personal experience is presented. Mortality, complications, and results are discussed.

The final conclusion is that esophagocoloplasty by means of the transverse colon in an intrathoracic and intrapleural position is a valuable method for re-establishment of the transit between the cervical esophagus and the stomach or jejunum in the treatment of caustic atresia, cancer, and varices of the esophagus.

REFERENCES

1. Kelling, G.: Oesophagoplastie mit Hilfe des Quercolon, Zentralbl. Chir. **38**: 1209-1212, 1911.
2. Mattos Barretto, P.: The Treatment of Cicatricial Atresia of the Esophagus, Tercer Congreso Panamericano de Otorrinolaringologia e broncoesofagologia, Havana, 1952.
3. Montenegro, E. B., Almeida, A. D., Vitali, E., and Rosa, J. C.: Behavior of the Colic Mucosa in the Presence of Gastric Juice. To be published.
4. Montenegro, E. B., Cutait, D. E., Ramos de Oliveira, M., Fanganiello, M., Faria, S. G., and Morgante, P. A.: Transthoracic Esophagoplasty for Benign Stricture by Means of the Transverse Colon, SURGERY **34**: 313-318, 1953.
5. Orsoni, P., and Lemaire, M.: Technique des esophagoplasties par le colon transverse et descendent, J. Chir. **67**: 491-505, 1951.
6. Vulliet, H.: De l'esophagoplastie et des diverses modifications, Semaine med. **31**: 529-530, 1911.

COMPARATIVE RESISTANCE OF THE ESOPHAGUS TO ACID AND PEPSIN

Relationship to Esophagitis Following High Esophagogastrostomy

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INTRODUCTION

A DISTRESSINGLY high incidence of esophagitis and its complications follows resection of the cardioesophageal junction with anastomosis of stomach to esophagus. Based upon clinical observations, it has been noted in the literature that esophagitis is rare following extensive esophageal resections with esophagogastrostomies performed high in the thorax in contrast to similar intrathoracic anastomoses placed near the diaphragm.[1-4, 11, 13] As a consequence, more extensive esophageal resection with esophagogastrostomy has been recommended as a better method of restoring gastroesophageal continuity with less chance of developing postoperative esophagitis. In commenting upon this observation and the value of high esophagogastrostomy, Sweet[11] recently stated in part: "It is possible that the mucosa of the middle, and particularly the upper portions, of the esophagus is much more resistant to the effects of irritating substances which bathe its surface. That such may be the case is suggested by the observation that postoperative esophagitis just above the esophagogastric anastomosis, following resection of the distal portion of the esophagus with preservation, in each instance, of the major portion of the stomach is less likely to develop when a long segment has been removed than after limited resections of the lower end."

As part of an investigation into several aspects of reflux esophagitis, this study was undertaken to test the concept that a difference in mucosal sensitivity per se may exist between the upper and lower areas of the intrathoracic esophagus. Both parts of the intrathoracic esophagus of dogs were exposed to various mixtures of HCl and pepsin. In addition, histologic studies of a limited number of normal canine and human esophagi were examined in an effort to find any difference in mucosal structure or mucous gland distribution between these 2 areas. The results of the animal experiments are presented with pertinent clinical observations relating to the subject based upon experiences with 8 patients who have had esophagectomy with high esophagogastrostomy.

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METHODS AND MATERIALS

Adult mongrel dogs weighing 20 to 35 pounds were used. Intravenous pentobarbital sodium was used for anesthesia and respiration was maintained through an endotracheal tube by a positive pressure respirator. Under sterile conditions a long left lateral thoracotomy incision was made, permitting the chest to be entered separately through the third and eighth intercostal spaces. The eighth intercostal space was opened first. The esophagus just superior to the diaphragm was gently mobilized and opened by a short longitudinal incision.

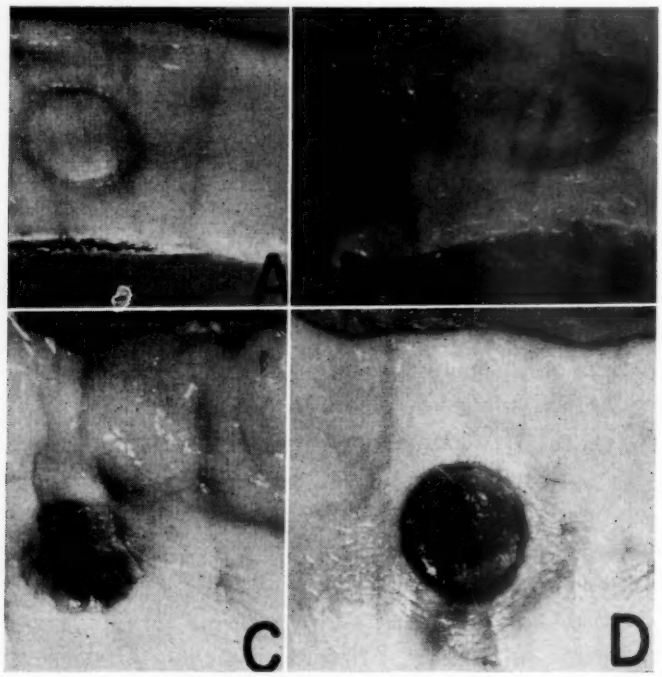

Fig. 1.—Immediate appearance of esophagi following exposure to HCl and pepsin. Representative segments selected to help illustrate gross classification. *A*, 1 plus, blanched with loss of luster. *B*, 2 plus, reddish congestion. *C*, 3 plus, opaque gray-brown. *D*, 4 plus, black. (Changes more apparent in natural color.)

Several attempts were made to expose a localized area of esophageal mucosa to a controlled drip or stream of acid-pepsin solution as have been described in studying mucosal resistance in other more mobile areas of the intestinal tract.[6-8] Because of difficulties in obtaining uniform exposures without spillage and the desire to avoid undue mobilization of the esophagus, a different method was devised for maintaining localized contact between mucosa and acid-pepsin solution free from the influence of swallowed saliva. A hollow glass tube with smoothly rolled open ends, 14 cm. long with an internal diameter of 12 mm., was placed vertically through the longitudinal incision into the esophagus and held in a vertical position. The underlying esophageal mucosa was held lightly against the tube's bottom opening by the operator's finger placed beneath the mobilized esophageal segment. An assistant then introduced 4 c.c. of solution into the open top end of the tube with a syringe. At the end of 3 minutes, the

solution was quickly aspirated by a special suction tip that avoided direct contact with the mucosa at the bottom of the tube. A second assistant immediately added another 4 c.c. of the same solution. Frequent irrigations were done to minimize the effects from the film of surface mucus.

At the end of this time the gross appearance of the exposed mucosa was graded by all observers as follows: 0—no change, 1 plus—blanched with loss of luster, 2 plus—reddish congestion, 3 plus—opaque gray-brown, and 4 plus—black (Fig. 1). The esophageal incision was closed with interrupted silk sutures and the eighth intercostal incision approximated. The third intercostal space was then entered and a segment of esophagus between the aortic arch and the apex of the chest opened. This supra-aortic part of the esophagus was then exposed to the same solution as the lower part using the identical technique.

Most animals were sacrificed at 24 to 48 hours postoperatively, but selected ones were allowed to survive for 4, 7, and 14 days. The animals were given nothing by mouth for the first 48 hours; thereafter, the diet was gradually increased from fluids to full kennel ration. Daily intramuscular penicillin was administered for 5 days. At autopsy the gross appearance of the esophagus was carefully noted, selected photographs taken, and the specimens prepared for histologic study.

Thirty-three dogs were divided into 5 groups on the basis of different exposures to HCl and pepsin (Table I). Three additional animals were exposed to physiologic saline to serve as controls. A solution of 0.1 normal HCl and 1 per cent pepsin was used in the largest number of animals since this closely approximates normal canine gastric secretions with a pH 1.2.[6] Solutions were freshly prepared using powdered pepsin, N.F., 1:3,000, before testing each animal.

TABLE I

	NUMBER OF DOGS	ESOPHAGEAL MUCOSAL REACTION	
		UPPER	LOWER
Group I	10	2+	2+
0.1 N HCl and 1 per cent pepsin	2	3+	3+
	1	4+	4+
	1	1+	1+
	2	2+	1+
	2	3+	2+
	1	4+	3+
	1	4+	2+
Group II	2	3+	3+
0.2 N HCl and 2 per cent pepsin	1	3+	2+
Group III	4	4+	4+
0.5 HCl and 5 per cent pepsin	1	3+	4+
Group IV	2	4+	4+
0.5 N HCl			
Group V	2	1+	1+
5 per cent pepsin			
Control	3	0	0
Physiologic saline			

Four fresh dog esophagi and 6 normal post-mortem human esophagi were studied by hematoxylin and eosin and mucicarmine staining techniques to detect any histologic difference in the structure or mucous gland pattern of the supra-diaphragmatic and supra-aortic areas.

RESULTS

The immediate effects of exposure to the various solutions are presented in Table I. Fourteen of 20 dogs exposed to physiologic 0.1 normal HCl and 1 per cent pepsin solution had equal mucosal reactions in both segments of the esophagus. Of the remaining 6 dogs, 5 had a mild difference in reaction, and in the sixth the difference was more marked. In the latter animals the reaction appeared to be somewhat less pronounced in the lower esophagus. The immediate reaction in both segments of the esophagus tended to become more pronounced with stronger solutions of HCl and pepsin. The reaction to 5 per cent pepsin without the addition of HCl was minimal in 2 dogs tested, whereas in 2 animals exposed to 0.5 normal HCl alone the reaction was marked. The control group showed no effect from contact with physiologic saline.

The black discoloration noted with 4 plus reactions immediately following exposure disappeared by 48 hours leaving a rough and reddened surface (Fig. 2). At 7 days areas of mucosal regeneration were visible on gross inspection. By 14 days the defect appeared to be almost completely covered. In no instance was there progression of the reaction through the muscular layer.

Histologically the early reaction (24 to 48 hours) was that of an acute esophagitis involving the mucosal and submucosal layers. In the most marked reactions the mucosa was destroyed and an acute inflammatory infiltration extended throughout the submucosa to the adjacent muscular coat. Edema and loss of cellular detail were present throughout the submucosa (Fig. 3). Outlines of the mucous glands remained in almost all severe reactions. Mucosal regeneration was nearly complete histologically at 14 days in the 4 plus reactions, but the resolving inflammatory reaction was still visible in the submucosa. In the milder reactions the inflammatory response and loss of structural detail were less marked.

DISCUSSION

Although the method described is not comparable to the continuous acid-pepsin exposure to which the human esophagus may be subjected, it did provide a single standardized reproducible means of maintaining contact between acid-pepsin solution and the esophageal mucosa free from the immediate effects of saliva. The 2 animals exposed to a more concentrated solution of HCl alone had a marked superficial chemical reaction, whereas pepsin without acid produced only a minimal reaction. In general the harmful effects of gastric secretions upon the esophageal mucosa are due to the combined action of pepsin in the acid medium of HCl.

Except for minor variations, there appeared to be no significant difference in the reactions of upper and lower canine esophagi when exposed to acid and

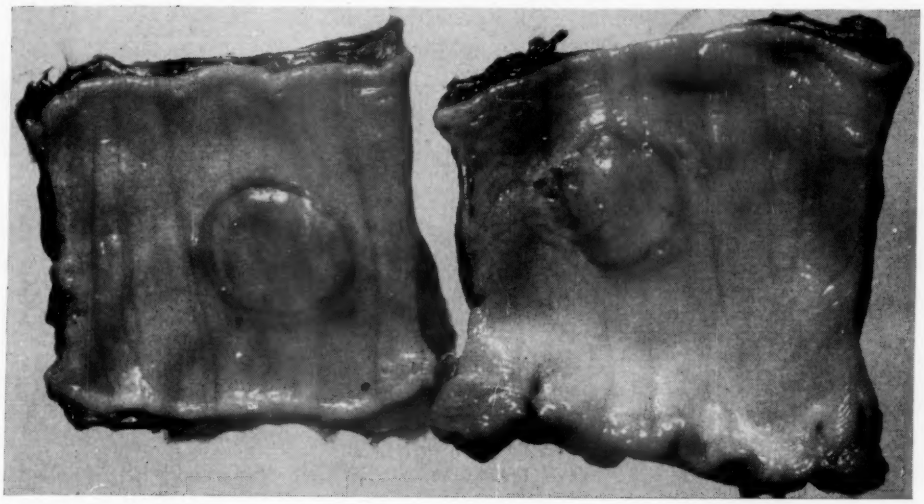

Fig. 2.—Segments from upper (*left*) and lower (*right*) esophagus of dog 48 hours following exposure to physiologic HCl and pepsin. Both had immediate 4 plus reactions. Earlier black discoloration gone; roughened red surface remains (see text).

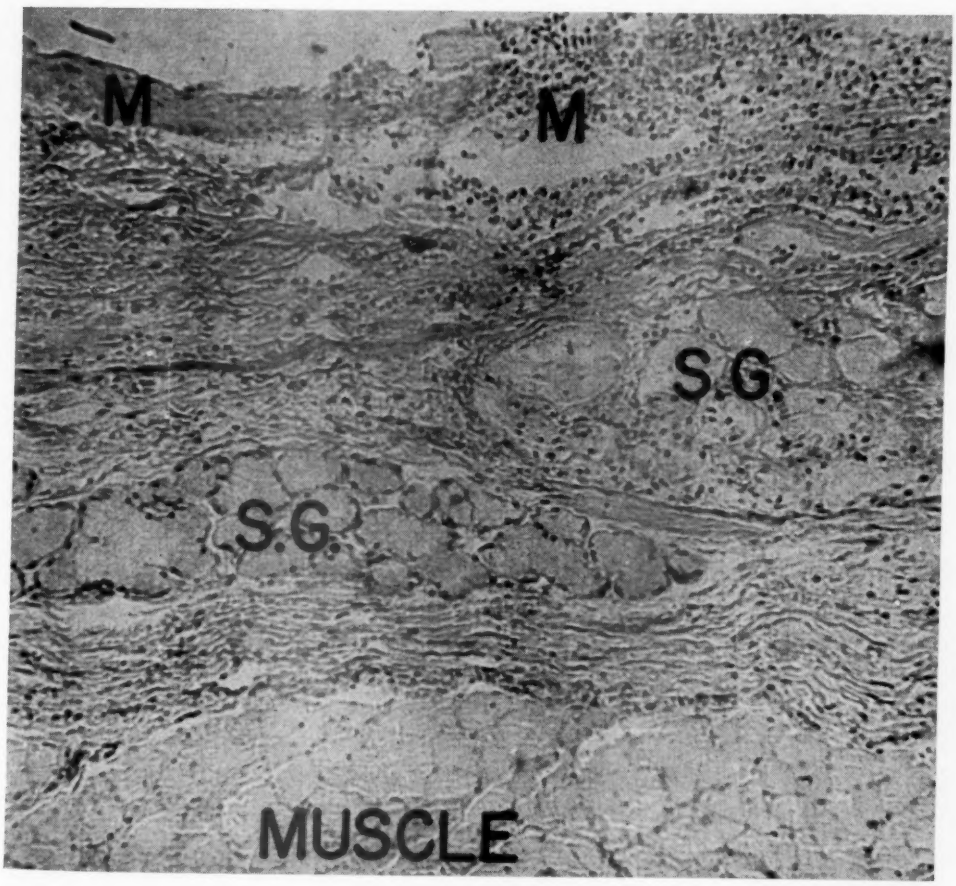

Fig. 3.—Representative photomicrograph (× 100) of dog esophagus 48 hours following an immediate 4 plus reaction to HCl and pepsin. Approximate junction of exposed (*right*) and unexposed (*left*) esophagus. Mucosa (*M*) destroyed and acute inflammatory reaction extends through the submucosa to the muscle layer. Outlines of swollen homogeneous submucosal mucous glands (*S.G.*) remain. Esophagus on left appears essentially normal except for slight mucosal reaction from the adjacent inflammation.

pepsin solutions by our method. In a recent report by Plzak, Fried, and Woodward,[10] studying mucosal sensitivities throughout the intestinal tract, there was no difference in reaction of the canine esophagus exposed to streams of HCl and pepsin solution in the areas "7 cm. distal to the cricoid cartilage" and "1 to 2 cm. proximal to the cardiac sphincter."

An observation of interest in our study was the wide variation in the reactions of the esophagi among individual animals exposed to freshly prepared physiologic acid-pepsin solution. The meaning of this difference in individual sensitivity is not clear. Perhaps it may be similar to the variations in esophageal reaction to gastroesophageal reflux seen among humans. Even with the most severe reactions, however, healing was in an advanced stage by 2 weeks. This again demonstrates the ability of the esophagus to recover from a single relatively superficial injury. Continuous or repeated insults of this type appear to be necessary to produce severe permanent changes and scarring.

On histologic examination there was no notable difference in the structure of the mucosa and mucous glands of the upper and lower intrathoracic areas of normal canine and human esophagi. In 2 human specimens, one or two islands of columnar mucosa were seen histologically 1 to 2 cm. above the junction of squamous and columnar epithelium. Occasional cardiac glands were noted in the distal segment of the esophagus. Apparently this transitional zone would not normally extend significantly into the supradiaphragmatic area of the esophagus. Of passing interest was the observation that dogs had many more mucous glands distributed throughout their esophagi.

If the scattered clinical impressions on the rarity of esophagitis and its complications following high esophagogastrostomy are really true, perhaps factors other than a difference in mucosal sensitivity per se may operate. To study this further, a small number of high intrathoracic esophagogastrostomies were performed in dogs following esophagectomy. The dogs generally did not tolerate an almost total intrathoracic stomach well, and the observations in this group of animals are inconclusive. However, we have had personal experience with 2 children with extensive lye strictures of the esophagus treated by esophagectomy and high esophagogastrostomy[9] now followed for 8 years postoperatively with no clinical evidence of esophagitis. Unfortunately, the parents would not permit esophagoscopy during a recent intensive evaluation.[5] An additional 6 patients with carcinoma of the mid-thoracic esophagus treated by esophagectomy and high intrathoracic esophagogastrostomy have been observed. Although none of these patients developed the classical symptoms of distress and heartburn so often associated with esophagitis in the lower esophagus, this does not exclude the possible occurrence of reflex esophagitis. Because a number of the high esophagogastrostomies reported have been performed for carcinoma of the esophagus, it should be emphasized that these patients comprise an older age group. Our patients with carcinoma of the esophagus had an average age in the sixth decade, a time when the acidity and proteolytic activity of the gastric secretions may normally be diminished. Another practical consideration is that the patients with esophageal carcinoma seldom live beyond one or 2 years

after surgery; no patient in our group lived beyond 2 years. Therefore, these patients may die before the clinical picture of esophagitis and its complications have had time to develop to an extent that would attract clinical attention.

Several other observations in our patients with high intrathoracic esophagogastrostomies deserve comment. When studied fluoroscopically by oral barium at a late postoperative date, the stomach was commonly noted to have assumed a straightened, rather tubular form and it emptied remarkably fast. All patients except one had a pyloromyotomy performed at the time of surgery because of the vagotomy resulting from esophageal transection. Several patients were studied in various positions after swallowing 3 fine polythene tubes with radiopaque tips. The tubes were fused together and positioned so as to measure pressures from the intrathoracic stomach at the diaphragmatic and mid-thoracic levels and from the esophagus within the apex of the chest. Pressures from each tube were recorded simultaneously through Statham strain gauges on a multichannel recorder (Electronics for Medicine). Intrathoracic pressure changes with breathing and coughing were reflected equally from all sites. There was no evidence of any significant pressure differential across the site of the esophagogastrostomy. It was of interest that a moderate increase in abdominal pressure by manual compression had little effect upon the totally intrathoracic stomach as compared to what one may see in the intrathoracic portion of the stomach with similarly increased abdominal pressure when most of the intact stomach lies below the diaphragm following a low intrathoracic esophagogastrostomy or with an incompetent hiatal hernia. Increased abdominal pressure, therefore, may be a factor favoring gastroesophageal reflux with low esophagogastrostomy in contrast to the almost total intrathoracic stomach of high esophagogastrostomy which is exposed to the same negative intrathoracic pressure as the adjoining esophagus. Nevertheless, patients with high esophagogastrostomies not uncommonly experienced eructation of sour fluid into their throats when they lay flat, especially in the early postoperative period. This free reflux of gastric contents into the esophagus with the supine position is not unexpected since there is no real resistance to this gravitational flow. An occasional patient will experience this sour reflux with sudden increases in intrathoracic pressure associated with violent coughing. The rapidly emptying narrowed stomach seen at a later period may lessen this tendency for gastroesophageal reflux.

Although the esophageal sensitivity studies in the dog cannot be transferred directly to the human, there is no reason to expect that a difference in mucosal sensitivity per se should exist between the upper and lower human esophagus. It is apparent that a number of other factors may operate in the production or prevention of gastroesophageal reflux and esophagitis following high esophagogastrostomies. Certainly no absolute clinical dictates can be drawn from the somewhat limited observations presented. However, complications following high esophagogastrostomy such as those noted by Sweet[12] may be more common than often suspected and reflux esophagitis may be the underlying mechanism of their production.

It should be questioned whether or not a more extensive esophagectomy with high esophagogastrostomy is a truly effective method for re-establishing gastroesophageal continuity following excision of benign and malignant lesions localized to the cardioesophageal area in the hope of preventing postoperative reflux esophagitis. The merits of this procedure will need to be evaluated against other techniques available, such as interposition of jejunum or colon between stomach and esophagus, various forms of gastric resection with or without drainage procedures, and the methods for reconstructing functioning cardioesophageal valves.

SUMMARY AND CONCLUSIONS

1. A difference in mucosal sensitivity between upper and lower esophagus has been suggested as an explanation for the clinical observation that esophagitis is rare following extensive esophagectomy with high esophagogastrostomy. Using the method described in this study, no significant difference in mucosal sensitivity between the upper and lower intrathoracic areas of canine esophagi was observed following exposures to HCl and pepsin. Of interest was the individual difference in the mucosal reactions among dogs exposed to identical solutions of physiologic HCl and pepsin.

2. Pertinent observations on 8 patients—2 who had lye strictures and 6 who had esophageal carcinomas—with esophagectomies and high intrathoracic esophagectomies are discussed. Pressure manometric studies indicate that the high almost total intrathoracic stomach is less affected by increased abdominal pressure than the stomach only partially above the diaphragm. Nevertheless, gastroesophageal reflux may occur with the high intrathoracic stomach from coughing, gastric distention associated with eating, and horizontal positions favoring upward gravitational flow from stomach to esophagus. These undesirable effects of high esophagogastrostomy may improve with time as the stomach becomes more tubular and empties faster. Esophagitis may appear to be uncommon in the carcinoma patients, but this may be misleading because of the discouragingly short postoperative survival period. In addition, these patients are in an advanced age group when gastric acidity and proteolytic activity are commonly decreased. Obviously factors other than mucosal sensitivity per se operate in the production of reflux esophagitis after high and low esophagogastrostomy.

3. It is questionable whether extensive esophagectomy with high esophagogastrostomy should be selected as the method for establishing esophagogastric continuity in the hope of preventing esophagitis following resection of most lesions localized in the cardioesophageal area.

REFERENCES

1. Burford, T. H., and Lischer, C. E.: The Treatment of Short Esophageal Hernia With Esophagitis by Finney Pyloroplasty, Ann. Surg. **144**: 647, 1956.
2. Cooley, D. A., and DeBakey, M. E.: Esophagectomy for Bleeding Esophageal Varices, A. M. A. Arch. Surg. **68**: 854, 1954.
3. DeBakey, M. E., and Cooley, D. A.: Palliative Resection for Carcinoma of the Esophagus, A. M. A. Arch. Surg. **66**: 781, 1953.
4. Husfeldt, E.: Hiatal Hernias, Acta chir. scandinav. **103**: 467, 1952.

5. Jewett, T. C., Jr., Carberry, D. M., and Adler, R. H.: Metabolic Effects of an Intrathoracic Stomach on the Growing Child, J. Thoracic Surg. In press.
6. Kiriluk, L. B., and Merendino, K. A.: The Comparative Sensitivity of the Mucosa of the Various Segments of the Alimentary Tract in the Dog to Acid-Peptic Action, SURGERY **35:** 547, 1954.
7. Kolouch, F., Jr.: A Direct Visual Technique for Studying Chemical and Other Injury to Exposed Mucosal Surfaces, SURGERY **17:** 641, 1945.
8. Le Veen, H. H.: Chemical, Physiological and Pathological Observations on the Role of Pepsin and Hydrochloric Acid in the Production of Experimental Ulcers, Gastroenterology **8:** 648, 1947.
9. Paine, J. R.: Excision of Extensive Lye Strictures of the Esophagus, New York J. Med. **51:** 2628, 1951.
10. Plzak, L. F., Jr., Fried, W., and Woodward, E. R.: Relative Susceptibility of the Gastrointestinal Tract to Experimental Acute Peptic Ulceration, S. Forum **7:** 389, 1956.
11. Sweet, R. H.: A Consideration of Certain Benign Lesions of the Esophagus, SURGERY **40:** 447, 1956.
12. Sweet, R. H., Robbins, L. L., Gephart, T., and Wilkins, E. W., Jr.: The Surgical Treatment of Peptic Ulceration and Stricture of the Lower Esophagus, Ann. Surg. **139:** 258, 1954.
13. Valdoni, P.: Traitement radical des stenoses oesophagiennes: la prevention de l'oesophagite peptique post operatoire, Presse méd. **59:** 1216, 1951.

GASTRIC ULCER

Survey of the Rhode Island Hospital Cases in the Ten-Year Period From 1946 Through 1955

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GASTRIC ulcer represents a clinical entity which has posed a problem both in diagnosis and treatment. The accepted form of therapy was to set forth a given length of time under medical management to allow healing of the gastric ulcer. Surgery was often not considered until the failure of medical management had been demonstrated. As more information about gastric ulcer was collected, with its intricate relationship to its malignant variety, the recent trend in therapy has altered. Surgery is being advised earlier by most, often as the initial step in treatment by some. It is clear now that, where gastric ulcers were once classified together with duodenal ulcers under the general category of peptic ulcer, different factors are at work in the genesis and natural history of either type. This paper represents a clinical and statistical survey of gastric ulcers, benign and malignant, seen and treated at the Rhode Island Hospital in the 10-year period from 1946 through 1955.

CASE MATERIAL

For the purposes of this paper, all cases of frank gastric carcinoma have been excluded. The study includes only those cases in which a diagnosis of gastric ulcer, benign or malignant, was made. Four hundred and sixty-nine benign and 50 malignant ulcers comprise the 519 total cases noted in the period under study. Total hospital admissions in the same period were 150,146, representing an incidence of 0.34 per cent or one case for every 289 admissions.

In this study only those cases of perforation in which the gastric origin of the perforation could be definitely identified were included. In many instances the site of the lesion was so close to the pylorus that the surgeon could not be certain of the actual location. All such cases have been excluded and the 52 perforations included in the group will not represent a true incidence of occurrence. Since perforations do not relate to the ulcer-cancer problem in the strictest sense, they will not be further considered except to note that, of the 52 cases recorded, 8 deaths resulted, 3 in cases treated medically and 5 following operation for closure of perforations.

It is a matter of passing interest to note that there were 297 private cases opposed to 222 ward cases over the entire 10-year period, with the ward cases falling from a percentage of 58 per cent in the first 5-year period to 28 per cent in the second 5-year period.

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Of the 519 cases, 142 were treated medically and 377 surgically (Table I).

TABLE I. 519 CASES OF GASTRIC ULCER, 469 BENIGN (90.4 PER CENT) AND 50 MALIGNANT (9.6 PER CENT)

TREATMENT	1946-1950	1951-1955	TOTAL
Medical	66	76	142
Surgical	*135*	*242*	*377*
Total	201	318	519
Percentage operated upon	67	76	73

Ages at admission ranged from 15 to 94, with 60 per cent of the patients in the 51 to 70 years age group. The average age was 58 years in the entire group, slightly lower than this figure for benign ulcers and slightly higher in the malignant group. The sex incidence was about three times as large in men (71 per cent) as in women (29 per cent). Of the 50 patients with malignant ulcers 33 (66 per cent) were men with the remaining 34 per cent women (Table II).

TABLE II. AGE AND SEX

AGE (YEARS)	BENIGN ULCER	MALIGNANT ULCER	SEX	BENIGN ULCER	MALIGNANT ULCER
10 to 30	16	2	Male	331	33
31 to 40	36	1	Female	138	17
41 to 50	87	8			
51 to 60	128	13			
61 to 70	135	17			
71 to 80	63	8			
81 and over	4	1			

Duration of symptoms in the entire group averaged 4.7 years. Combining this figure with the average age of 58 years, you obtain an average age of onset of symptoms of 53.3 years. Compare this figure with duodenal ulcer patients in whom the average age at onset is usually taken at 30 years of age and it will readily be seen that gastric ulcer and duodenal ulcer are diseases of different age groups. Duration of symptoms in the malignant ulcer group averaged 1.3 years, a very significant figure compared to the average for the entire group.

It is striking to note that there was no difference in significant weight loss (10 pounds in a 6-month period) in the benign and malignant groups. Thirty-one per cent of the benign ulcer group showed weight loss compared to 36 per cent for the malignant ulcer groups.

Hemorrhage of some type occurred in the history of 38 per cent of the benign group and 35 per cent of the malignant ulcer group. Massive hemorrhage occurred in 11 per cent of the benign group and 4 per cent of the malignant group. Four per cent of the benign group were admitted with pyloric obstruction, but one-half of these cases also had an associated duodenal ulcer. Only one case of pyloric obstruction (2 per cent) was noted in the malignant ulcer group.

Multiple ulcers or duodenal ulcer in the presence of a gastric ulcer are generally considered strongly suggestive of a benign lesion. Thirty-one patients in the series had multiple gastric ulcers; all of these occurred in the benign group. Fifty-two of the benign ulcer group had an associated duodenal ulcer for an incidence of 11 per cent, while 3 (6 per cent) of the malignant ulcer group had an associated duodenal ulcer. A survey of the literature bears out the rarity of the co-existence of malignant gastric ulcer and duodenal ulcer. This was not confirmed by this study. There is an appreciable incidence of the development of gastric malignancy following gastroenterostomy for duodenal ulcer to such an extent that most authors strongly urge that any ulcerating gastric lesion following gastroenterostomy be closely scrutinized before recommending medical management (Table III).

TABLE III

	BENIGN ULCER	MALIGNANT ULCER
Weight loss	31%	36%
Hemorrhage	38%	35%
Massive hemorrhage	11%	4%
Pyloric obstruction	19	1
Multiple ulcers	31	0
Associated duodenal ulcer	52	3

GASTRIC ANALYSIS

Histamine stimulation was used in the majority of those cases tested for free acid. Of the 469 benign ulcers, 179 were tested for free acid with 14 per cent showing absence of free acid. Of the 50, in the malignant ulcer group 30 were tested and achlorhydria was found in 36 per cent. This latter figure may seem significant, but the incidence of achlorhydria in the benign ulcer group (14 per cent) is sufficiently high to detract from the value of this test as a diagnostic tool. The average age of the patients in the benign group showing no free acid was 57, while that of the malignant group was 61 years, which makes the figures even less significant because there is an accepted rate of achlorhydria in the normal elderly patient. Forty-seven per cent of benign ulcers showed free acid values of greater than 40 degrees, while 24 per cent of the malignant ulcers showed free acid values of greater than 40 degrees. (Table IV.)

TABLE IV

FREE ACID	BENIGN ULCER	MALIGNANT ULCER
(0) Units	25 (14%)	11 (36%)
5 to 20	25	1
21 to 40	48	6
41 and over	81 (47%)	12 (24%)

GASTROSCOPY

Gastroscopy was performed in only 4 per cent of the 519 patients studied. The gastroscopic diagnosis was verified by pathologic examination in only 7 of the 20 benign ulcers gastroscoped and one of the 3 malignant ulcers. In

8 of the remaining 15, gastroscopy was reported as negative where a lesion was found by pathology. One instrumental perforation occurred in this group. Only 6 of the 23 gastroscopies were performed in the second 5-year period, which is indicative of the reliance the staff members of this hospital place on the procedure. Too few cytologic smears of stomach aspirate were performed on our patients for evaluation. Conclusions from other such studies have shown up to a 10 per cent false-positive and a 35 per cent false-negative incidence.

X-RAY EXAMINATION

Much has been written concerning the radiographic differentiation of benign and malignant ulcer. In recent years, with resections becoming more and more frequent, a more accurate estimation of error in clinical diagnosis has now become possible. In determining the accuracy of the radiologist in this study, x-ray reports were divided into 3 groups: (a) those reported as benign, (b) those reported as malignant, and (c) those reported as questionable. The latter group includes those where no definite opinion was given or where the report could "not exclude the possibility of malignancy."

Three hundred and one of the 519 cases had gastrointestinal series performed at this hospital. One hundred and sixty-one were reported as benign with a final pathologic correlation of 93.8 per cent. Of the 47 reported as malignant, 36 proved to be benign for an x-ray accuracy of only 23.4 per cent. In the 93 cases reported as questionable, 79 per cent of these proved to be benign. (Table V.)

TABLE V. PATHOLOGY

X-RAY REPORT	BENIGN ULCER	MALIGNANT ULCER	PER CENT CORRECT
Benign	151	10	93.8
Malignant	36	11	23.4
Questionable	73	20	

Thus when a gastric ulcer is called benign, the accuracy of diagnosis is 93.8 per cent, whereas where the roentgenologic diagnosis is malignant, the accuracy falls to only 23.4 per cent. Benign ulcers are therefore more likely to appear malignant on x-ray visualization. This is further borne out by the number of benign lesions in the questionable group. The over-all x-ray accuracy on both benign and malignant lesions was 78 per cent, which is only slightly lower than the 85 to 90 per cent quoted by other authors, some of whom concede an irreducible 10 per cent range of error in x-ray diagnosis. It is interesting to note that when a surgeon in our series diagnosed a lesion at operation grossly as benign he had an accuracy of 94.2 per cent, which is quite similar to the roentgenologic accuracy. When he called the lesion malignant his accuracy fell to 63 per cent. Again grossly as well, the benign lesion is the one more likely to masquerade as malignant.

SIZE OF LESION

The size of the lesion is of some importance. In this study, the size range of the ulcer is shown in Table VI.

TABLE VI

SIZE (CM.)	BENIGN ULCER	MALIGNANT ULCER
0.0-1.0	106	7 (6%)
1.1-2.0	101	10 (8%)
2.1-3.0	30	8 (21%)
3.1-4.0	13	9 (22%)
4.1-5.0	9	7 (43%)

It can be seen that as the size of the ulcer increases the percentage of benign ulcer decreases, while the percentage of malignant ulcer increases. It has been previously pointed out that lesions over 2.5 cm. in diameter were strongly indicative of malignancy. This is not strictly true except in comparison with the smaller lesions. It is also striking to note that the largest ulcers in our series were benign. Five benign ulcers were greater than 6 cm. in diameter, while only one malignant ulcer was 6 cm. in diameter. Only 6 per cent of the lesions 1 cm. or less were malignant, whereas 43 per cent of those over 4.1 cm. were malignant. Although the size of the ulcer is of some help in determining the presence of malignancy, it cannot be taken as a reliable point in the differential diagnosis of the individual lesion.

LOCATION OF LESIONS

The location of benign and malignant lesions as found at operation or autopsy is outlined in Table VII. These include 293 benign and all 50 malignant ulcers. Grouping all gastric ulcers together there were more benign ulcers in all areas than malignant ones, but in certain areas like the antrum the incidence of malignant lesions rose to 22 per cent, while malignant lesions of the pylorus and fundus, as reported, were only rare. Fifteen per cent of the lesions located on the greater curvature were malignant; 4 of the total 5 malignant greater curvature lesions were situated in the media. In the past the incidence of malignancy in greater curvature lesions was felt to be a good deal higher, but our series, as well as those of Smith and Jordan (12 per cent) and Marshall (16 per cent), have shown the actual incidence to be similar to the over-all incidence for any location in the stomach. (Table VII.)

TABLE VII

TYPE	BENIGN		MALIGNANT		PER CENT
LOCATION	G. C.	L. C.	G. C.	L. C.	MALIGNANT
Pylorus	2	8	0	0	0
Prepyloric	7	85	1	15	15
Antral	5	37	0	12	22
Media	11	131	4	17	13
Fundus	2	5	0	1	12

G. C.—Greater curvature.
L. C.—Lesser curvature.

TREATMENT METHODS

Of the 519 patients, 142 (27 per cent) were treated by medical management only. The reasons for this were varied and in many cases could not be clearly ascertained from the individual records. These included excellent response in healing to a trial period of ulcer therapy, advanced age, concomitant

disease, patients' refusal to submit to surgery, and, in the case of massive bleeding, condition so poor as to preclude surgery. In addition, some of these patients who were treated medically only on their Rhode Island Hospital admissions went to have surgery for their problem elsewhere.

For these and other reasons, follow-up studies were incomplete in this study. The main difficulty, other than the above, lay in losing patients referred to the outpatient department or discharged to the care of their own physician. These factors would make it unwise to derive any conclusions based upon the treatment statistics to be presented (Table VIII).

TABLE VIII

	MEDICAL TREATMENT	SURGICAL TREATMENT
Cases	142	377
Deaths	17	25
Mortality	12%	6.6%

Of the 142 patients treated medically, a mortality of 12 per cent was encountered. The 17 deaths included 12 patients dying from hemorrhage so severe as to prevent their being brought into condition for surgery. Perforation and ensuing peritonitis accounted for 3 deaths. One patient died from cardiac decompensation, and one death occurred in the malignant ulcer group; this patient proved at autopsy to have liver metastases.

In evaluating the results of medical therapy, approximately 60 per cent of patients treated medically in the hospital were discharged with x-ray evidence of healing of the ulcer. It is interesting to note that in 4 cases x-ray evidence of healing was noted and the patient went on to operation at a later date, at which time a malignant ulcer was found.

Surgical therapy of some type was carried out in 377 patients (73 per cent) of the entire group. The indication for operation was for hemorrhage in 15 per cent, question of malignancy in 60 per cent, and perforation in 15 per cent. Duodenal ulcer, cholelithiasis, and other miscellaneous causes accounted for the remainder.

Subtotal gastrectomy of some type was carried out in 318 patients, 23 of these being Billroth I procedures. There were 3 gastroenterostomies, 11 excisions of gastric ulcer, one in the malignant group, and 5 exploratory laparotomies, all in the malignant group. The remaining operations consisted of 49 closures of perforated gastric ulcers. (Table IX.)

TABLE IX

OPERATION	BENIGN ULCER	MALIGNANT ULCER
Subtotal gastrectomy	279	39
Billroth I	20	3
With omentectomy	15	14
Gastroenterostomy	1	2
Excision of ulcer	11	1
Exploratory laparotomy	0	5
Total gastrectomy	0	2
Closure of perforation	49	0

There were 25 deaths (an over-all mortality of 6.6 per cent); 20 of these were in the benign and 5 in the malignant group (Table X). Five deaths followed surgery for perforated ulcer.

TABLE X. POSTOPERATIVE DEATHS

CAUSE	NUMBER	AGE (YEARS)	NUMBER
Peritonitis	11	20 to 30	0
Hemorrhage	5	31 to 40	2
Myocardial infarct	3	41 to 50	2
Pulmonary embolism	2	51 to 60	4
Hepatorenal	2	61 to 70	11
Acute bacterial endocarditis	1	71 to 80	6
Enterocolitis	1	80 and over	0

One patient died from persistent bleeding following excision of a benign bleeding gastric ulcer. One of the two total gastrectomy patients succumbed to peritonitis on the tenth postoperative day, while the other was discharged on the eighth postoperative day after receiving radioactive gold therapy in addition. Four patients required operative intervention in the course of massive hemorrhage and died postoperatively. This leaves a total of 13 deaths for 314 subtotal gastrectomies performed electively for gastric ulcer, or an operative mortality of 4.1 per cent for that procedure alone—11 in the benign and 2 in the malignant group. This figure can now be compared with those in Table XI.

TABLE XI. ELECTIVE SUBTOTAL GASTRECTOMY FOR GASTRIC ULCER

		CASES	OPERATIVE MORTALITY
Walters et al.	1952	157	2.2%
Priestley et al.	1952	178	4.9%
Lahey and Marshall	1953	221	3.1%
Wallenstein et al.	1953	364	2.2%
Gothman et al.	1953	103	1.7%
R. I. Hospital	1955	314	4.1%

Again lack of follow-up material makes it impossible to evaluate the results of the surgical therapy. We can note that there were 6 cases of carcinoma-in-situ in our series and, of these, 4 have a survival of 5 years or more.

Complications of some type occurred in approximately 30 per cent of the cases. The most common complications were local wound pathology-infections and dehiscence—and pulmonary pathology including atelectasis, bronchopneumonia, and embolism. Distribution of the postoperative days is shown in Table XII.

TABLE XII

POSTOPERATIVE DAYS	BENIGN ULCER	MALIGNANT ULCER
0 to 10	166	24
11 to 20	135	15
21 and over	33	6

SUMMARY

An attempt has been made to survey the gastric ulcer problem as it occurs in a community hospital of this size. The case material and incidence of gastric ulcer have been outlined. Patients' ages and duration of symptoms were presented. Factors such as weight loss, hemorrhage, pyloric obstruction, multiple or associated duodenal ulcers, and gastric analysis were compared in both the benign and malignant groups. Our experience with the accuracy of gastroscopic and radiologic techniques has been discussed. Pathologic characteristics of size and location were determined and compared. Our methods of treatment and resulting complications during hospitalization were analyzed.

A further follow-up study is in progress.

CONCLUSIONS

1. The problem of gastric ulcer is a common one occurring in one out of every 289 hospital admissions.

2. The duration of symptoms in the malignant group proved to be shorter, averaging 1.3 years, as compared to 4.7 years for the entire group of gastric ulcers.

3. There is no difference in significant weight loss in the benign and malignant ulcer patients.

4. Massive hemorrhage occurs more frequently in benign than in malignant gastric ulcers but can occur in approximately 4 per cent of the malignant group.

5. The presence of a duodenal ulcer does not rule out malignancy in an associated gastric ulcer. Six per cent of our malignant ulcer group had an associated duodenal ulcer. Multiple gastric ulcers were associated only with benign lesions in our series.

6. A significant number (14 per cent) of benign gastric ulcer patients are found to have achlorhydria on routine examination, and a significant number (24 per cent) of the malignant ulcer patients have elevated acid values. Therefore, this determination cannot be considered a reliable diagnostic tool.

7. Gastroscopy has been unreliable in our experience.

8. Radiologic techniques in the differentiation of benign and malignant ulcers will probably not exceed an accuracy of 90 per cent.

9. As the size of a gastric ulcer increases, the chance of its being malignant also increases. However, in our series the 5 largest ulcers, all over 6 cm. in diameter, were benign.

10. Benign ulcers are more common in all areas of the stomach compared to the malignant ones. Approximately one out of 5 lesions of the antrum, excluding the prepyloric area, was malignant. One out of 7 ulcers in the prepyloric area proved to be malignant.

11. It is well known and borne out by this study that malignant ulcers can demonstrate x-ray evidence of healing under medical management.

12. A high rate of minor complications (30 per cent) and an operative mortality of 4.1 per cent in elective subtotal gastrectomy for gastric ulcers were noted in this study.

REFERENCES

1. Deutsch, Emmanuel: Gastroscopy, New England J. Med. **250**: 468-476, 1954.
2. Marshall, S. F.: The Relation of Gastric Ulcer to Carcinoma of the Stomach, Ann. Surg. **137**: 891-903, 1953.
3. Myers, H. C.: Early Diagnosis of Carcinoma of the Stomach, J. A. M. A. **163**: 159-161, 1957.
4. Rhoads, J. E.: Preventive Surgery in the Field of Cancer, Ann. Surg. **146**: 782-789, 1957.
5. Schumaker, F. V., and Hampton, A. O.: Radiologic Differentiation of Benign and Malignant Ulcers, Ciba Symposium **8**: 23-34, 1956.
6. Smith, F. H., and Jordan, S. M.: The Problem of Gastric Ulcer Reviewed, J. A. M. A. **153**: 1505-1508, 1953.
7. Welch, C. E., and Allen, A. S.: Gastric Ulcer, New England J. Med. **240**: 277-283, 1949.

A NEW TECHNIQUE OF PYLOROPLASTY

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THE purpose of this article is to report a new method of pyloroplasty which effectively increases the diameter of the pylorus. The procedure is simple to perform and is believed to increase the efficiency of gastric drainage following vagotomy. The operation was done first experimentally on 9 dogs of which 7 survived the anesthetic and surgical procedure. Its clinical application has been limited to 8 patients with most encouraging results. The proposed method, to our knowledge, has not been previously reported in the literature.

The technique is essentially a modification of the Y-plasty procedure used for stricture of the ureteropelvic junction. It varies only in that the upper part of the Y takes the shape of a U to assure adequate vascularity at the most distal portion of the gastric flap. The U portion of the Y is placed in the anterior surface of the stomach, just proximal to the pyloric ring, while the stem of the Y continues caudally through the pyloric ring and into the duodenum for a distance equal to the length of the gastric flap. A single row of interrupted, nonabsorbable, gastrointestinal sutures is used to accomplish the pyloroplasty. A small flap of omentum is placed over the suture line and held in place with 2 or 3 sutures for greater security. In all our experimental and clinical experience with this procedure, there has never been a failure due to necrosis of the antral flap. The technique is illustrated in Fig. 1.

DISCUSSION

Table I shows actual measurements of the pylorus before and after the Y-plasty type of pyloroplasty on 9 dogs. Measurements of the diameter of the pylorus and duodenum were taken by means of graduated obturators. The obturator selected fit the bowel wall snugly but did not stretch the bowel wall. The pylorus was measured before and after pyloroplasty through a separate gastrotomy opening while the duodenum was measured through the Y-plasty incision.

It is noteworthy that in every instance except one, Dog 2, the diameter of the pylorus after Y-plasty was greater than the diameter of the duodenum. These measurements in Dog 2 were the same. There is nothing to be gained in enlarging the diameter of the pylorus beyond that of the duodenum.

The technique of pyloroplasty just described appears to have definite advantages over pyloroplasties of the Mikulicz[3] or Finney[1, 2] types and their numerous modifications.

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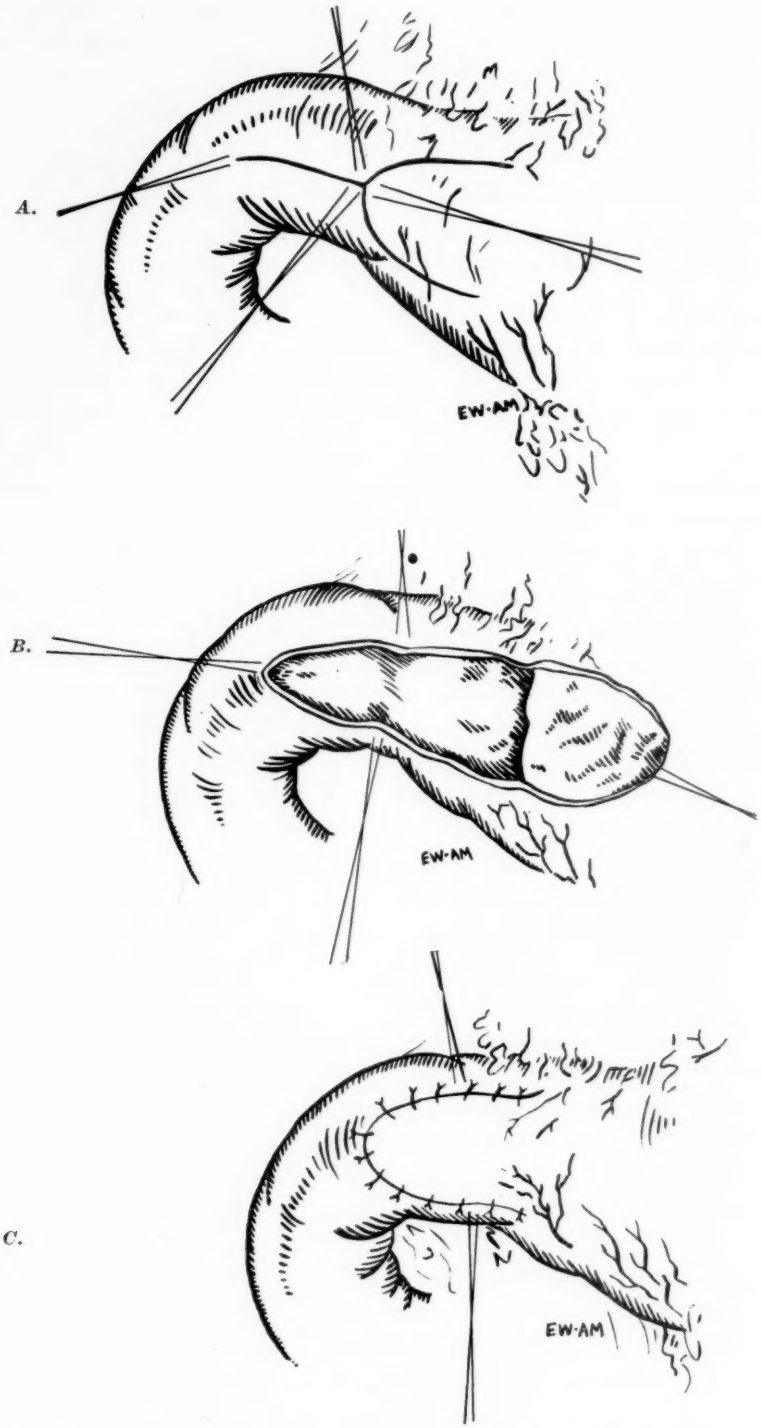

Fig. 1.—*A*, Lines of incision outlined with marking sutures in position. *B*, Y-incision completed. *C*, Y-plasty completed.

A.

B.

Fig. 2.—*A*, Barium meal before pyloroplasty. *B*, Barium meal 4 days after pyloroplasty.

TABLE I

DOG NUMBER	WEIGHT (LBS.)	PYLORUS*		DUODENUM*
		BEFORE	AFTER	
1	31	1.3	2.5	1.9
2	23	0.7	1.5	1.5
3	28	1.5	2.5	1.7
4	20	0.9	2.3	1.5
5	42	1.7	2.9	2.8
6	38	1.5	2.5	1.9
7	18	1.1	1.9	1.5
8	28	1.5	2.3	2.0
9	26	1.5	2.3	1.9

*Diameters measured in centimeters.

The Y-plasty technique effectively increases the diameter of the pylorus in a manner which avoids the "dog-ear"-like deformity of the pylorus, which is inherent in pyloroplasties of the Mikulicz and Finney type. Although the transverse diameter of the pylorus is markedly increased in the latter types of pyloroplasty, the "dog-ear" distortion of the pylorus may interfere with free emptying of the stomach.

The Y-plasty technique avoids time-consuming and sometimes hazardous mobilization of the pylorus and duodenum upon which the successful accomplishment of the Mikulicz and Finney pyloroplasties depend. It is applicable in the presence of active ulceration and in most cases where firm and dense adhesions exist about the pylorus. It utilizes pliable and abundant antral tissue which insures against faulty apposition of tissues and widely separates the two cut ends of the pyloric ring.

The 8 clinical cases, although few in number, have had no difficulty in gastric emptying after vagotomy and the Y-type of pyloroplasty. Fig. 2 demonstrates the area of pyloroplasty before and 4 days after surgery in our second clinical case. The channel is adequate and functional and shows no evidence of distortion. The 2-hour films show virtually complete emptying while the 4-hour films show complete emptying.

SUMMARY

A simple, yet effective, new method of pyloroplasty has been presented and its apparent advantages over other methods have been discussed. Its successful use in 8 cases of chronic duodenal ulcer is reported.

REFERENCES

1. Finney, J. M. T.: A New Method of Pyloroplasty, Bull. Johns Hopkins Hosp. **13**: 155, 1902.
2. Finney, J. M. T., and Friedenwal, J.: Fourteen Years' Experience With Pyloroplasty, Surg., Gynec. & Obst. **18**: 273, 1914.
3. Mikulicz, J.: Zur operativen Behandlung des stenosirenden Magengeschwüres, Arch. klin. Chir. **37**: 79, 1888.

THE EFFECT OF CABBAGE FACTOR ON THE PEPTIC ULCER OF MANN-WILLIAMSON DOGS

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THE observation that one or more essential dietary factors affect the occurrence of peptic ulcer in experimental animals has been known for many years. In 1921 McCarrison reported that gastric ulcers developed in 33 per cent of guinea pigs fed a diet consisting of oats and cooked milk and later reported that prolonged administration of this diet resulted in duodenal ulcers and even perforation.[21, 22] Smith and McConkey[25] found that 26 per cent of guinea pigs fed a vitamin C-deficient diet developed duodenal ulcers very similar to those occurring in man, and Jensen[17] showed that rats on a diet deficient in vitamin A developed gastric ulcers.

Nutritionists have been aware for some time that lack of an unknown dietary factor or factors led to gizzard erosions in chicks. Almquist and Stokstad[2] showed that this factor was a fat-soluble substance present in lettuce, cabbage, other greens, and milk, and after it was supplied the erosions healed rapidly. Almquist and Mecchi[1] also found that bile acids, especially cholic acid, were effective dietary supplements in preventing gizzard erosions in chicks. Earlier reports that duodenal ulcers occurred in dogs and other animals when the biliary drainage was externally diverted support these findings. Blanck[4] reviewed this problem in 1935 and reported on 8 dogs with complete external biliary drainage. Three were refed bile and did not develop ulcers but the other 5 did. Emery and Schnitker[14] treated 40 ulcer patients with desiccated ox bile and found that seasonal recurrence could thus be prevented in 73 per cent of patients. In 1942 Cheney, working with chicks in which he induced gastric ulcers by administration of cinchophen, found that such ulcers could be prevented by supplying an anti-gizzard-eroding factor which he called vitamin U, the substance being a heat labile sterol found in alfalfa and milk.[6] Another factor seemed to be involved in chick gizzard erosions, for Bird and associates demonstrated the effectiveness of chondroitin in their prevention and suggested that its glucuronic acid content was primarily responsible.[3] These authors pointed out that green plant materials were poor sources of chondroitin. Five years earlier Crandall and Roberts[13] found that, of a series of patients with duodenal ulcers treated with chondroitin, 45 per cent showed definite symptomatic improvement in 7 days.

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Working with a "grass juice factor" essential to guinea pig growth and weight maintenance, Elvehjem's group[18, 19] found that a basal casein diet without this factor led to the occurrence of severe stomach ulcers and decreased weight and growth. These adverse occurrences were fully correctable with dried grass. Subsequent work by this group[16] led to the conclusion that the various effects of the "grass juice factor" must have been produced by counteracting amino acid and mineral deficiencies. Specifically, arginine was proved to be the principal limiting factor in the basal ulcerogenic casein diet and certain grasses were shown to contain large amounts of this amino acid.

The most extensive experimental and clinical testing of the antiulcer dietary factor found in vegetable greens was done by Cheney[7-12] who in a series of papers reported the effectiveness of a heat-labile factor, a fat-soluble sterol, found in lettuce, cabbage, and parsley. He called this substance vitamin U. Cabbage was selected as a readily available source and he showed that the whole leaf, raw juice, or concentrate was effective in varying degrees in preventing histamine ulcers in guinea pigs and in healing peptic ulcers in man. However, this enthusiasm has not been shared by others and in carefully controlled clinical studies Brooks and associates[5] found no significant difference between the rate of healing of duodenal ulcers as determined by roentgen methods in patients treated with cabbage juice concentrate and those receiving a placebo.

Further laboratory evaluation seemed indicated and cabbage juice concentrate was tried on the peptic ulcer of the Mann-Williamson dog.

METHOD

Twenty adult mongrel dogs ranging in weight from 10 to 26 Kg. were utilized in this study. They were operated upon under intravenous Nembutal anesthesia and a Mann-Williamson procedure was carried out. The duodenum was divided just distal to the pylorus and the duodenal stump was closed. The proximal small bowel was divided 30 inches from the pylorus. The distal end of the divided jejunum was anastomosed to the pylorus of the stomach. The proximal limb of jejunum was anastomosed end-to-side to the ileum 30 inches proximal to the ileocecal junction. The animals were given penicillin and streptomycin intramuscularly and maintained on intravenous fluids for 3 postoperative days and were then gradually returned to their previous diet of canned horse meat and biscuit rations in equal amounts ad libitum, the latter incorporating minerals, vitamins A and D, brewers' yeast, liver meal, and wheat germ.

On the tenth postoperative day, 10 of the animals were given orally 6.5 c.c. of cabbage juice concentrate (Merck Sharp & Dohme, Inc., MK79) before the daily meal. This was equivalent to one liter of fresh cabbage juice and was administered daily for 40 days. The dogs were weighed weekly and fasting samples of gastric juice were aspirated on the tenth, thirtieth, and fiftieth postoperative day and analyzed for free hydrochloric acid.

The surviving dogs were sacrificed on the fiftieth postoperative day, and all animals dying before the end of the experiment were immediately autopsied.

The gastrointestinal tract was carefully examined and specimens from the anastomoses as well as from the duodenum, small bowel, and colon were taken for histologic examination after staining with hematoxylin and eosin. Ulcers were measured and classified as to whether they were restricted to the bowel wall or displayed penetration or perforation of the jejunum. The 10 control dogs had similar operations, management, and studies.

RESULTS

The results of the findings in the control animals and the animals in the group treated with cabbage juice concentrate is summarized in Table I. All animals fed cabbage juice survived the 50 days of the experimental period and were sacrificed, revealing 4 penetrating jejunal ulcers and the absence of ulceration in 2 dogs. In the control groups 3 dogs' ulcers perforated and they died. Of the surviving animals, four had penetrating ulcers and in one dog no jejunal ulcer was found. All ulcers occurred in the usual location within 1 to 2 cm. of the gastrojejunal anastomosis. The size and appearance of the ulcers in the two groups were not significantly different. One dog treated with cabbage juice concentrate had 2 ulcers while all others had a single ulcer. It was noted that a number of animals had gastric dilatation even though the gastrojejunal anastomosis was patent and allowed passage of the index finger easily.

TABLE I

DOG NUMBER	ULCER (CM.)	PENETRATING OR PERFORATING	DIED* (DAY)	WEIGHT (LBS.)			BODY WEIGHT LOSS (PER CENT)
				INITIAL	FINAL	LOSS	
			Control Group				
925	2 × 3	Penetrating	--	29.0	16.2	12.8	44.2
741	1 × 1	--	--	40.0	28.5	11.5	28.7
1078	2 × 2	Perforating	42nd	27.0	15.1	11.9	44.1
1431	1.2 × 1.5	Perforating	19th	28.0	20.1	7.9	28.2
1430	1.5 × 2	Penetrating	--	27.0	16.1	10.9	40.0
1384	1.5 × 2.2	Penetrating	--	27.1	20.4	6.7	24.7
251	None	--	--	34.9	21.1	13.8	39.6
618	1 × 2	--	--	30.4	20.0	10.4	34.2
670	0.8 × 1	Perforating	31st	30.5	19.6	10.9	31.1
1250	1.5 × 2	Penetrating	--	29.0	21.2	7.8	26.9
						Average	34.2
			Cabbage Juice Concentrate-Treated Group				
930	None	--	--	30.0	24.1	5.9	19.7
738	1.4 × 1.9	Penetrating	--	34.3	27.0	7.3	21.3
1237	1 × 1	--	--	37.0	19.4	17.6	47.6
1234	0.5 × 1.5 1.5 × 1.5	--	--	33.0	22.3	10.7	32.4
929	1.5 × 2.4	Penetrating	--	30.0	24.4	5.6	18.7
40	None	--	--	29.0	25.1	3.9	13.4
997	1.5 × 3	Penetrating	--	34.0	20.9	13.1	38.6
619	1 × 3	--	--	30.0	21.0	9.0	30.0
838	1 × 2	Penetrating	--	29.0	19.1	9.9	34.1
718	1.5 × 2	--	--	37.0	26.4	10.6	28.6
						Average	28.4

Tabulation of ulcer size, number, and type in dogs in control and cabbage juice concentrate treated groups. Note lesser morbidity and weight loss in treated group.

*All living animals were sacrificed on the fiftieth postoperative day. The animals which died are indicated as to the postoperative day this occurred.

All dogs lost weight rapidly after the Mann-Williamson procedure. Weight loss varied from 13.4 per cent of body weight (in a dog treated with cabbage juice concentrate which did not develop an ulcer) to 47.6 per cent in both groups. The dogs treated with cabbage juice concentrate lost 28.4 per cent of body weight and the control group 34.2 per cent.

Interval gastric analyses assaying for free hydrochloric acid and total acid showed no significant differences between control group and animals given cabbage juice concentrate.

Tissue sections taken through the ulcer-bearing areas of the control and treated series showed no significant differences when these areas were compared as to epithelization, fibroplasia, and vascularity. The other sections of the bowel appeared normal. Both groups showed the ulcer to be severe, usually involving all coats of the jejunal wall. Little or no tendency for epithelization was observed and, in addition to the necrosis and inflammatory reaction, fibroplasia and increased vascularity of varying degrees were noted.

DISCUSSION

Cabbage juice concentrate appears to contain a factor or factors that may alter the morbidity and mortality following the Mann-Williamson procedure in dogs. It has been reported to aid in the healing of peptic ulcer in man[9-12] but other workers have not confirmed this finding.[5] The identification of this "antiulcer" factor is still being pursued and recently new impetus has been given to the investigations by the work of Shive and co-workers.[24] Initially they had isolated a heat-labile methyl sulfonium derivative of methionine from cabbage juice but subsequent clinical studies indicated that this was probably not the antiulcer factor. Further work has indicated that glutamine may be the active principle. This is also heat labile and found in large amounts in cabbage juice. A preliminary study dealing with 57 peptic ulcer patients given 1.6 Gm. of glutamine daily (the amount in one liter of cabbage juice) suggested a beneficial effect.

Recently Heinicke and associates[16] reported studies dealing with the protein and amino acid requirements of the guinea pig. They indicated that the peptic ulcers which occurred in these animals when on a basal casein diet were due to an arginine deficiency.[18, 19] From these investigations it appears that amino acids may play a role in the genesis of peptic ulcer.

Cheney[10] suggested that vitamin U may act by increasing the resistance of the gastrointestinal mucosa to erosion by hydrochloric acid and pepsin. Although our interval gastric analyses showed no conclusive difference in free or total gastric acid between treated and control groups, Fauley and Ivy[14] point out that mere titration of the acidity of gastric contents in Mann-Williamson dogs is not indicative of available acid for attacking the jejunal mucosa, for quantity of acid and duration of contact are important factors for consideration.[15]

Cheney's clinical results are based upon the time at which pain relief occurred and ulcer crater healing took place by x-ray, claiming an average

crater healing time of 13.4 days for 134 patients treated with cabbage juice compared to 49.9 days for 295 patients treated with conventional medical therapy. This is in considerable disagreement with Rossett and Knox[23] who reported an average healing time of 15 days for 506 patients with proved duodenal ulcers. These authors also point out that the reliability of making a diagnosis of the healing of a duodenal ulcer by x-ray is about 50 per cent.

In a more recent study using a double blind control Cheney evaluated 45 patients treated for 22 days with cabbage juice concentrate or a placebo. He utilized x-ray once a week for his evaluation and claimed that 32 per cent given a placebo healed at the end of the period compared to 92 per cent of those receiving cabbage juice concentrate.[12]

Brooks and his group[5] treated 21 patients with demonstrated duodenal ulcer craters for 3 weeks; 10 received cabbage juice concentrate and 11 received a placebo. They noted no significant difference between the two groups in disappearance or decrease of epigastric pain, subsidence of epigastric tenderness, or change in crater size. Interestingly, they found a transient inhibition of gastric hydrochloric acid response to histamine or insulin after intragastric administration of cabbage juice extract to duodenal ulcer patients.

Since the concentration of the various constituents already isolated from cabbage juice in the search for the elusive antiulcer factor vary considerably due to natural differences in soil, climate, and so forth, it is conceivable that a true and as yet unrecognized active factor may be present and that these variations in cabbage juice may account for the repeated differences in its clinical effectiveness.

SUMMARY

1. The experimental evaluation of cabbage juice antiulcer factor on the peptic ulcer of Mann-Williamson dogs is reported. Clinical interest in this method of treatment of peptic ulceration in man warranted further experimental work.

2. Cabbage juice concentrate equivalent to one liter of fresh cabbage juice was given orally to 10 dogs for 40 days starting on the tenth postoperative day following a Mann-Williamson procedure. Ten control Mann-Williamson dogs were also studied. All dogs that survived were sacrificed on the fiftieth postoperative day.

3. Among the dogs treated with cabbage juice concentrate two failed to develop an ulcer, four developed penetrating ulcers, and all survived to the end of the experiment. Among the controls, one failed to develop an ulcer, 3 had ulcers that perforated and died, and 4 developed penetrating ulcers.

4. The control animals lost an average of 34.2 per cent of their weight and the animals given cabbage juice concentrate lost 28.4 per cent.

5. Comparison of interval gastric analyses, and microscopic examination of the ulcers revealed no significant differences between the control group and treated groups.

6. Further investigation of the role of dietary factors and especially of amino acids in the etiology and treatment of peptic ulcers seems indicated.

We wish to thank Dr. I. S. Ravdin for his guidance in this study and Dr. John T. McGrath, Associate Professor of Veterinary Pathology of the School of Veterinary Medicine of the University of Pennsylvania, for assistance in the evaluation of the microscopic sections in this study.

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REFERENCES

1. Almquist, H. J., and Mecchi, E.: Influence of Bile on Erosions of Chick Gizzard Lining, J. Biol. Chem. **126:** 407, 1938.
2. Almquist, H. J., and Stokstad, E. L.: Gizzard Factor of Chick, J. Nutrition **13:** 339, 1937.
3. Bird, H. R., Oleson, J. J., Elvehjem, C. A., and Hart, E. B.: Effectiveness of Chondroitin in Preventing Gizzard Erosion in Chicks. J. Biol. Chem. **126:** 671, 1938.
4. Blanck, E. E.: Peptic Ulcer. An Experimental Study, Surg., Gynec. & Obst. **61:** 480, 1935.
5. Brooks, F., and Machella, T.: The Effect of Cabbage Juice Concentrate on Peptic Ulcer in Man. To be published.
6. Cheney, G., Cinchophen Gastric Ulcers in Chicks, Arch. Int. Med. **70:** 532, 1942.
7. Cheney, G.: The Nature of the Anti-Peptic-Ulcer Dietary Factory, Stanford Med. Bull. **8:** 144, 1950.
8. Cheney, G.: Prevention of Histamine-Induced Peptic Ulcers by Diet, Stanford Med. Bull. **6:** 334, 1948.
9. Cheney, G.: Rapid Healing of Peptic Ulcers in Patients Receiving Fresh Cabbage Juice, California Med. **70:** 10, 1949.
10. Cheney, G.: Vitamin U Concentrate Therapy of Peptic Ulcer, Am. J. Gastroenterol. **21:** 230, 1954.
11. Cheney, G.: Vitamin U Therapy of Peptic Ulcer, California Med. **77:** 248, 1952.
12. Cheney, G., Waxler, S. H., and Miller, I. J.: Vitamin U Therapy of Peptic Ulcer: Experience at San Quentin Prison, California Med. **84:** 39, 1956.
13. Crandall, L. A., Jr., and Roberts, G. M.: Observations on Administration of Chondroitin in Peptic Ulcer, Proc. Soc. Exper. & Biol. **30:** 704, 1933.
14. Emery, E. S., and Schnitker, M. A.: Peptic Ulcer: The Effect of the Administration of Bile on the Behavior of the Disease, Ann. Int. Med. **11:** 2007, 1937.
15. Fauley, G. B., and Ivy, A. C.: The Prevention of Postoperative Jejunal Ulcers by Diet and Fundusectomy, Surg., Gynec. & Obst. **63:** 717, 1936.
16. Heinicke, H. R., Harper, A. E., and Elvehjem, C. A.: Protein and Amino Acid Requirements of the Guinea Pig, J. Nutrition **57:** 483, 1955.
17. Jensen, J. L.: The Effect of Tocopherols in Preventing Gastric Ulcers in Rats, Science **103:** 586, 1946.
18. Kohler, G. O., Elvehjem, C. A., and Hart, E. B.: The Relation of the Grass Juice Factor to Guinea Pig Nutrition, J. Nutrition **15:** 445, 1938.
19. Kohler, G. O., Randle, S. B., Elvehjem, C. A., and Hart, E. B.: Simplified Rations for Guinea Pigs Suitable for Assay of the Grass Juice Factor, Proc. Soc. Exper. Biol. & Med. **40:** 154, 1939.
20. Mann, F. C., and Williamson, C. S.: The Experimental Production of Peptic Ulcer, Ann. Surg. **77:** 409, 1923.
21. McCarrison, R.: Some Surgical Aspects of Faulty Nutrition, Lancet **1:** 1151, 1931.
22. McCarrison, R.: Studies in Deficiency Disease, New York, 1921, Oxford University Press, p. 95.
23. Rossett, N. E., Knox, F. H., and Stephenson, S. L.: Peptic Ulcer. Medical Cure by Efficient Gastric Acid Neutralization, Ann. Int. Med. **36:** 98, 1952.
24. Shive, W., Snider, R. N., DuBilier, B., Rude, J. C., Clark, G. E., Jr., and Ravel, J. O.: Glutamine in Treatment of Peptic Ulcer. Preliminary Report, Texas J. Med. **53:** 840, 1957.
25. Smith, D. T., and McConkey, M.: Peptic Ulcers (Gastric, Pyloric, and Duodenal): Occurrence in Guinea Pigs Fed on Diet Deficient in Vitamin C, Arch. Int. Med. **51:** 413, 1933.

MESENTERIC ARTERIAL INSUFFICIENCY

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ARTERIOSCLEROSIS severe enough to compromise the arterial flow to the intestine could conceivably give rise to abdominal pain or decreased intestinal function resulting in constipation[4] and postprandial distention.[17] Countless people die with occlusion of the femoral and popliteal arteries in whom the diagnosis is never made because the occlusion did not result in gangrene. When gangrene is present, however, attention is quickly directed to the arteries as being the primary site of disease. The same may be true of mesenteric occlusion, previous attention having been focused only on those instances in which ischemia was so severe as to result in infarction of the bowel or in which generalized arterial disease suggested superior mesenteric artery involvement.[1, 3, 12] Partial mesenteric occlusion, like partial popliteal occlusion, may present a syndrome of limited exercise tolerance or decreased function with various degrees of pain.[25]

This study represents an effort to explain, in part, the physiologic changes occurring in the gastrointestinal tract associated with arteriosclerosis. A study has been made of the anatomic changes of the superior mesenteric artery of humans associated with various degrees of arteriosclerosis. Specifically, it is a study of the cross sectional area of the superior mesenteric artery of 75 human beings.

The cross sectional area was calculated from the diameter measurements which were always made in 3 places (Fig. 1). The diameter measurements were made (a) at the aortic opening, (b) at the narrowest segment, which was invariably 0.25 to 1.0 cm. distal to the aortic opening, and (c) 1.5 cm. distal to the aortic opening where the vessels were usually pliable and free of arteriosclerotic changes. Measurements were obtained with the aorta in situ and after removing the aorta with its branches. The elastic tissue contained in the aorta resulted in a shrinkage which varied from 8 to 28 per cent, depending upon the severity of arteriosclerosis. In general, it was observed that the greater the arteriosclerotic involvement the less the shrinkage upon removal.

Twenty-eight of the 75 aortas studied demonstrated narrowing of the superior mesenteric artery varying from 12 to 86 per cent of the cross-sectional area with an average of 28 per cent. The arteriosclerotic narrowing consistently occurred just distal to the aortic opening of the superior mesenteric artery.

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In those instances where the aorta and its branches are still elastic, subsequent study indicates that the inelastic point of narrowing is accentuated by the increased diameter of the vessels when subjected to systemic arterial pressures.[10]

A better yardstick for understanding the effect of narrowing may be gained from calculating the maximal theoretic flow limitations associated with various degrees of narrowing. According to Poiseuilles law, the pressure head remaining constant, then the velocity is directly proportional to the sectional area of the tube, but the quantity of fluid passing through the tube per unit of time (volume flow) is proportional to the fourth power of the diameter of the tube.

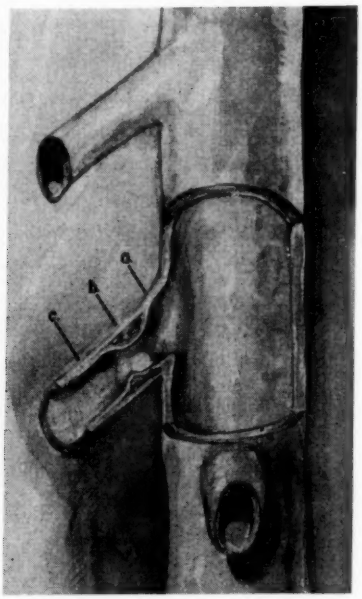

Fig. 1.—Sites of measuring vessel diameter. *a*, Aortic opening of superior mesenteric artery. *b*, Area of greatest narrowing. *c*, 1.5 to 2.0 cm. distal to aortic opening.

With the gradual occlusion of the superior mesenteric artery, as may occur in the aging process, several possibilities have been suggested. First, with gradual occlusion, a compromised blood supply may exist sufficient for bowel viability and for satisfactory function after light meals, but incompetent or lacking in sufficient functional reserve to handle large meals when the intestine is called upon to do a great deal of work.[6] Second, a gradual occlusion of the superior mesenteric artery may result in the establishment of collateral channels to an extent that bowel viability and bowel function are unimpaired even with heavy meals. Third, secondary occlusion of some of the smaller mesenteric vessels may occur so that small areas of intestinal infarction or perhaps only mucosal ulcers develop, giving only transient abdominal symptoms.[14] Fourth, sudden complete occlusion of the superior mesenteric artery without collateral channels having been established may result in necrosis of the bowel.[18]

Nazari[21] found 7 cases of complete arteriosclerotic closure of the superior mesenteric artery in 1,700 autopsies, and in only one case had intestinal infarction resulted. Blalock and Levy[5] reported that gradual occlusion of the celiac and mesenteric axis over a 3-month period was successful in some animals, indicating that potential collaterals are present, whereas sudden occlusion of the superior mesenteric vessels is consistently fatal.

Laufman and Method[16] found that with occlusion of the superior mesenteric artery for 2½ hours, secondary relaxation of the mesenteric vessels occurred and the bowel viability was seriously impaired. Nelson and Kremen[22] stated that the superior mesenteric artery or vein of the dog could be safely occluded for 2 hours and that antibiotics to reduce the intestinal flora extended the time of permissive occlusion. Similarly, heparin administered preoperatively in order to prevent intravascular clotting permitted extension of the time of occlusion.

Derr and Noer[9] in a series of experiments on dogs concluded that vascular deprivation of a bowel segment 15 cm. or less in length cannot be accomplished uniformly by interruption of intestinal arcuate vessels due to the collateral role of the intramural vessels. Rothschild[24] demonstrated in dogs the importance of the intramural and marginal artery in the collateral circulation of the bowel, pointing out that the degree of safety is far greater in man than in animal, a finding contrary to that of Noer.[23] Horsley and Coleman[13] found that in the dog a short segment of intestine may be deprived of its primary blood supply and still maintain its integrity by having the omentum wrapped around it.

The vicissitudes of the collateral channels which supply the intestine are not well defined nor are they well known. It is known, however, that once blood traverses a capillary bed the effective pressure it is capable of delivering is greatly reduced, the reduction apparently being related to the size of blood vessels delivering the blood through the collateral channel. Klein[14] demonstrated that gradual obliteration of either mesenteric artery was well tolerated until the arterial blood pressure distal to the occlusion was reduced to 20 per cent of normal. In the face of partial arterial occlusion, a secondary fall in arterial pressure precipitated by systemic causes such as congestive heart failure, shock, or distention secondary to intestinal obstruction may result in gangrene.

Elliott[11] was the first to report the successful surgical treatment for mesenteric vascular occlusion when in 1895 he resected 130 cm. of small intestines. Since then numerous surgeons have described successful massive intestinal resections for mesenteric occlusion, but often the amount of bowel involved was so extensive that little bowel remained to meet the nutritional requirements of the individual. Such patients were nutritional invalids as a result of the small amount of functional intestine remaining.

The feasibility of sacrificing the hepatic, superior mesenteric, or renal arteries and satisfactorily replacing them with other intra-abdominal arteries has been demonstrated in a series of dogs.[2] Perhaps the vascular frontier

has been advanced sufficiently so that partial occlusion of the superior mesenteric artery can now be diagnosed and the involved segment resected or bypassed.[19] The superior mesenteric artery 2 cm. distal to the aortic opening is very pliable and would therefore provide an adequate vessel for a graft or a bypass.

It may be that exploratory operations for gallbladder disease,[15] peptic ulcer, and suspected cases of carcinoma would not be performed if the symptom complex of intestinal arterial insufficiency were kept in mind and diagnostic means improved to facilitate accurate diagnosis. The unexpected poor result of intestinal surgery in older persons may at times be explained on the basis of arteriosclerotic mesenteric arterial insufficiency.

SUMMARY

The cross-sectional area of the superior mesenteric artery has been studied in 75 unselected necropsies. Detailed measurements indicate that 28 of the 75 demonstrated some arteriosclerotic narrowing of the superior mesenteric artery, which varied from 12 to 86 per cent of the cross-sectional area. The point of narrowing occurred consistently at a point 0.25 to 1.0 cm. distal to the aortic orifice of the superior mesenteric artery.

The physiologic changes occurring in the gastrointestinal tract associated with mesenteric artery insufficiency are discussed.

It was a pleasure to have had the help and encouragement of Drs. Alton Ochsner and John Howard in pursuing this work.

REFERENCES

1. Allen, E. V., and Hausner, E.: Generalized Arterial Involvement in Thromboangitis Obliterans, Proc. Staff Meet., Mayo Clin. **15**: 7, 1940.
2. Altman, S., Borow, M., Hurwitt, E. S., and Rosenblatt, M.: Intra-abdominal Arterial Anastomosis, SURGERY **34**: 1043, 1953.
3. Barron, M. E., and Cohan, S. S.: Thromboangitis Obliterans With Special Reference to Its Abdominal Manifestations, New England J. Med. **26**: 1275, 1936.
4. Berman, L. G., and Russo, F. R.: Abdominal Angina, New England J. Med. **242**: 611, 1950.
5. Blalock, A., and Levy, S. E.: Gradual Complete Occlusion of the Celiac Axis, the Superior Mesenteric, and Inferior Mesenteric Arteries With Survival of Animals, SURGERY **5**: 175, 1939.
6. Councilman, N.: Three Cases of Occlusion of the Superior Mesenteric Artery, Boston Med. & Surg. J. **Cxxx P**: 410, 1894.
7. Cunningham, R. S.: The Physiology of the Serous Membranes, Physiol. Rev. **6**: 242, 1926.
8. Cuny, J.: Rupture d'un aneurysme de l'aorte abdominal simultant un volvulus du colon pelvicu, Chir. Lyon **34**: 58, 1937.
9. Derr, J. W., and Noer, R. S.: Experimental Mesenteric Vascular Occlusion, Surg., Gynec. & Obst. **89**: 393, 1949.
10. Derrick, J. R.: Unpublished data.
11. Elliott, J. W.: The Operative Relief of Gangrene of the Intestine Due to Occlusion of the Mesenteric Vessels, Ann. Surg. **21**: 9, 1895.
12. Garvin, E. J.: Mesenteric Vascular Occlusion Complicating Thromboangitis Obliterans, Am. J. Surg. **74**: 211, 1947.
13. Horsley, J. S., and Coleman, C. C.: Experimental Devascularization of Segments of Intestine With and Without Mechanical Obstruction, J. A. M. A. **59**: 597, 1912.
14. Klein, E.: Embolism and Thrombosis of the Superior Mesenteric Artery, Surg., Gynec. & Obst. **23**: 385, 1921.
15. Larson, L. M.: Mesenteric Vascular Occlusion, Proc. Staff Meet., Mayo Clin. **8**: 38, 1933.

16. Laufman, H., and Method, H.: The Role of Vascular Spasm in Recovery of Strangulated Intestine, Surg., Gynec. & Obst. **85**: 675, 1947.
17. Mayo, H. W.: Dissecting Aneurysm Simulating Large Bowel Obstruction, Am. J. Surg. **82**: 522, 1951.
18. Meyer, J. L.: Mesenteric Vascular Occlusion, Ann. Surg. **94**: 88, 1931.
19. Mikkelson, W. P.: Intestinal Angina, Am. J. Surg. **94**: 262, 1957.
20. Morse, L. J., Krynski, B., and Mulkeen, T. T.: Superior Mesenteric Vascular Occlusion, Am. J. Surg. **93**: 788, 1957.
21. Nazari, A.: Arteriosclerosi e occlusione delle arterie mesenterische, Policlinico **14**: 42, Roma 1907.
22. Nelson, L. E., and Kremen, A. J.: Experimental Occlusion of the Superior Mesenteric Vessels, SURGERY **28**: 819, 1950.
23. Noer, R. J.: The Blood Vessels of the Jejunum and Ileum, Am. J. Anat. **73**: 293, 1943.
24. Rothschild, N. S.: Safety Factors in Mesenteric Ligations, Ann. Surg. **89**: 878, 1929.
25. Shelly, H. S.: Dilatation of the Colon, Ann. Surg. **109**: 257, 1939.

MULTIPLE CANCERS IN COLON SURGERY

Report of 162 Cases

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SINCE Billroth[2] first directed attention to the possibility of more than one primary cancer's occurring in an individual, the phenomenon has aroused interest and speculation. Billroth's case report was published in 1869, but it was well over 50 years before physicians began to realize that this was neither a rare occurrence nor a medical curiosity. During the past 25 years many reports have appeared in the medical literature of the world, mostly single case reports, but a sizeable number have been careful reviews with large numbers of new cases. In spite of these more recent reports and careful studies by many authorities, too many physicians, while realizing the possibility of a patient's developing more than one cancer, are prone to lapse into the habit of ascribing all symptoms to a single disease process and thus overlook a second and possibly more malignant disease. The purpose of this report is to emphasize again the extreme importance of careful and thorough examination and investigation of all symptoms and signs presented by a patient; thus, by early and complete diagnosis and therapy the cancer mortality rates may continue to be lowered.

CRITERIA

The choice of adequate criteria for establishing the diagnosis of multiple primary malignancy is a controversial subject. Billroth's original postulates are stated often and are worthy of repetition. These are: each tumor must have an independent histologic appearance, the tumors must arise in different locations, and each tumor must produce its own metastases.[2] To these postulates Mercanton[11] added an additional requirement; after removal of each of 2 carcinomas, the patient remains free of the disease, thus demonstrating that the lesions were primary and not metastases. Billroth's criteria were too strict and ruled out many multiple primary malignancies. They did not admit the possibility of multiple primaries within a single organ such as the colon or the rectum.

Gradually, the requirements for diagnosis were liberalized as knowledge of cancer increased and histologic study became more precise. Long, Mayo, Dockerty, and Judd[10] pointed out that the microscopic appearance of a second neoplasm will determine whether it is a recurrence or a completely new growth by the type of transition from normal to malignant cells at the margins. After

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an extensive survey of cases of multiple malignancy, Warren and Gates[19] proposed the functional criteria which follow: each of the tumors must present a definite picture of malignancy, each must be distinct, and the possibility of one's being a metastasis of the other must be excluded. These criteria are generally accepted in this country, and we have adhered to these in the selection of our cases.

INCIDENCE

The possibility of development of two or more cancers, either in the same or in different organs, at the same time or at different times, is recognized by everyone; but the relative frequency of primary polycancers varies greatly from one author to another. Those authors with the lowest figures doubt if these lesions occur more often than expected by chance alone. Some years ago it was felt by authors such as Lockhart-Mummery,[9] Dukes,[5] and Cramer[4] that one malignant growth had an inhibitory effect upon the development of other primary malignant neoplasms in the same person. Excellent statistical data and numerous case reports now indicate that multiple primary cancers are found more often than would be expected from statistics based upon the general population, at least where the skin, the genitomammary system, and the large bowel are concerned. Mider and associates,[12] for example, found 133 multiple primary cancers of the breast and of the colon when statistical expectation had been 65. In 1954, Stenstrom and Ford[16] analyzed 1,000 cases of carcinoma of the colon and found 48 in which there were multiple primary carcinomas of the colon. Ginsburg and Dreiling[6] reported 25 instances of independent primary carcinomas developing in 700 patients having previous resections for colon malignancies (3.57 per cent).

TABLE I. RELATIVE FREQUENCY OF MULTIPLE PRIMARY MALIGNANCY

AUTHORS	TOTAL NUMBER OF CANCERS	PERCENTAGE OF MULTIPLE PRIMARIES
Muller[13]	1,121	1.8
Mider et al.[12]	276	2.89
Warren-Gates[19]	1,259	3.7
Brindley-Rice[3]	1,091	4.67
Owen[14]	3,000	4.7
Ward[17]	1,773	5.2
Warren-Ehrenreich[18]	2,828	6.8
Bacon-McGregor	1,788	9.1

In spite of the wide variations in incidence reported by various authors (Table I), there is an apparent increase in the reported incidence of multiple malignancy. This increasing reported incidence is due to the increasing knowledge in the diagnosis of malignancy, the improvements in the techniques of examination, particularly in the field of radiology, and the improvements in methods of therapy which have increased the frequency with which patients survive their original malignant process.

The frequency of multiple primary cancers will be much higher when based upon autopsy reports than when based upon clinical and operative findings

because of the limitations of these methods, but autopsy incidence must be accepted as the more reliable. Warren and Ehrenreich[18] found 23 multiple cancers of the bowel and 9 cases of combined lesions of the gastrointestinal tract in 69 autopsies performed on patients who had died of cancer of the large intestine. Hanlon[7] isolated 18 autopsy cases with multiple malignancies of which only 2 had been diagnosed clinically and radiologically.

In the 17½-year period from September, 1940, to May, 1958, 1,788 cases of microscopically verified cancer of the colon and the rectum have been admitted to the senior author's Proctologic Service. There have been 162 patients with multiple primary malignancies, an incidence of 9.1 per cent. Portions of this series have been reviewed in previous papers.[1]

DISTRIBUTION

The distribution of multiple primary lesions varies according to the author, but the most frequently reported sites are the skin, the breast, and the large bowel. The distribution of cancers in the same or in different systems offers much ground for discussion. Some authors state that multiple primary cancers have a definite tendency to group themselves in organs of the same anatomic system, while others believe that the systemic relationship is coincidental. Warren and Gates[19] found the colon to be the most frequent site for multiple carcinoma in a single organ. They found 55 cases of double carcinoma of the colon in 1,259 total cases. Hurt and Broders[8] found 9 of 71 multiple primary carcinomas to involve the colon. Stalker, Phillips, and Pemberton[15] located approximately 29 per cent of their series in the colon or in the stomach. Warren and Ehrenreich[18] cited 33 per cent of colon involvement alone and 14 per cent of associated lesions of the colon and other parts of the gastrointestinal tract.

In our 162 cases, there were 94 cases with multiple primary lesions of the large intestine alone, an incidence of 54.9 per cent of the cases of multiple malignancy and 5.3 per cent of the total number of cancer patients. We have excluded from this series those patients who had multiple malignant changes develop in intestinal polyposis or multiple adenomatosis of the colon. There were 68 cases (41.9 per cent) who had involvement of organs or systems other than the colon (Table II).

TABLE II. MULTIPLE PRIMARY MALIGNANCIES

	INVOLVEMENT OF LARGE INTESTINE ALONE		INVOLVEMENT OF LARGE INTESTINE AND OTHERS	
	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
Males	60	37.0	30	18.5
Females	34	21.0	38	23.5
Total	94	58.0	68	42.0
Total number of cancer patients			1,788	
Total number of multiple primary cases			162	(9.2%)
Number of systemic multiple primary cases			94	(5.3%)

For the 94 patients with systemic multiple primary cancers there were 201 lesions. The distribution of these lesions is shown in Table III. In this group there were 60 men and 34 women; thus, two-thirds of the total number of men

had lesions limited to the large bowel, while only 47 per cent of the women had only systemic lesions. In addition to the 60 men with lesions of the large bowel alone, there were 9 men with second or third primary cancers in the upper gastrointestinal tract. Only one woman in the entire series had a second carcinoma involving the upper gastrointestinal tract (Table IV). This implies a predisposition in men to multiple lesions of the gastrointestinal system.

There were 29 women in the series who had a second or third primary cancer in the genitomammary system, an incidence of 40 per cent of all women in

TABLE III. NUMBER OF LESIONS IN LARGE INTESTINE ALONE

SEX	RECTUM	SIGMOID	DESCENDING	ASCENDING	TRANSVERSE	CECUM
Men	70	45	3	4	7	3
Women	26	26	3	4	7	3
Total	96	71	6	8	14	6

Total number of lesions 201
Total number of cases 94

TABLE IV. NUMBER OF LESIONS IN GASTROINTESTINAL TRACT

SEX	LARGE INTESTINE	STOMACH	ESOPHAGUS	GALL BLADDER	TOTAL
Women	64	7	1	1	73 (81%)
Men	41	1	-	-	42 (58%)

TABLE V. MALIGNANCY OF THE LARGE BOWEL WITH PRIMARY MALIGNANT NEOPLASIA OF THE FEMALE GENITALS AND BREAST

NAME	AGE	SITE	GENITOMAMMARY ORGAN INVOLVED	ADDITIONAL SITES
M. M.	69	Sigmoid	Breast	
F. C.	50	Rectum	Uterus	
P. G.	41	Sigmoid	Uterus	Bladder
A. L.	72	Rectum	Breast	
E. L.	52	Rectum	Uterus	
L. R.	49	Rectum	Ovary	
L. S.	66	Sigmoid	Breast	Transverse colon
J. L.	42	Sigmoid	Breast	
B. D.	44	Rectum	Ovary	
N. B.	69	Rectum	Uterus	
R. W.	42	Rectum	Ovary	
W. C.	37	Rectum	Ovary	
M. K.	43	Sigmoid	Ovary (bilateral)	
J. J.	65	Rectum	Ovary	Pancrease
S. G.	65	Sigmoid	Breast	
L. S.	49	Sigmoid	Breast	
A. W.	65	Rectum	Breast	
P. C.	70	Rectum	Uterus	
M. R.	58	Rectum	Uterus	Transverse colon
V. A.	47	Sigmoid	Breast	
H. T.	32	Rectum	Ovary	
A. F.	51	Rectum	Uterus	
A. C.	70	Rectum	Ovary	
O. R.	61	Rectum	Uterus	
F. R.	83	Rectum	Breast	
E. S.	57	Rectum	Breast	
M. S.	65	Rectum	Breast	
P. W.	39	Rectum	Breast	
A. F.	77	Descending colon	Uterus	

the series. These patients and their lesions are shown in Table V. While the relationship between the female sex hormones and carcinoma of the breast and the female genital organs is well known, the effect of the hormones on the development of a second primary malignancy of the genitomammary system in the presence of a carcinoma of the large bowel may be theorized only. In this series the patients were mostly in the menopausal or postmenopausal age group, but this does not imply that estrogenic stimulation had ceased. Perhaps, in time, endocrinology will be an important factor in explaining carcinogenesis.

In our series the skin was involved by a second or third primary lesion in only 9 patients (5.5 per cent). This is considerably lower than in most reported series. The genitourinary system was the site for additional lesions in 15 cases (9.2 per cent). The distribution of lesions outside the large intestine is shown in Table VI.

TABLE VI. NUMBER OF LESIONS OUTSIDE THE LARGE INTESTINE

	GENITO-URINARY	GASTRO-INTES-TINAL	GENITO-MAM-MARY	SKIN	LUNG	TONGUE	LARYNX	PAN-CREAS	EYE
Men	9	9	1	5	1	2	2	–	1
Women	6	1	29	4	1	–	–	1	–
Total	15	10	30	9	2	2	2	1	1

Of the 162 patients in this series, 140 had 2 primary lesions; 22 had 3 lesions. Three of these 22 developed a fourth lesion, 2 of these subsequently developed a fifth lesion, and one a sixth lesion. This patient was a woman who developed 6 successive lesions, 4 of which involved the colon. The first was an adenocarcinoma of the splenic flexure (1943); the second, an adenocarcinoma of the rectum (1945); the third, an endometrial carcinoma of the uterus (1951); the fourth, squamous-cell carcinoma of the forehead (1952); the fifth, an adenocarcinoma of the splenic flexure (1955); and the sixth, an adenocarcinoma of the cecum found on exploration associated with extensive metastasis (1957).

SUMMARY AND CONCLUSIONS

A review of the literature has been made to reveal the importance of the entity of multiple primary malignancies. A consecutive series of 1,788 cases of carcinoma of the rectum and the colon have been reviewed. Of these cases, 162 had multiple primary cancers, an incidence of 9.2 per cent. Multiple primary cancers of the large bowel alone were noted in 5.3 per cent. It was seen that men show a definite predisposition to involvement of the gastrointestinal tract. In this series, 67 per cent of men had their lesions confined to the gastrointestinal tract. The genitomammary system was involved in 40 per cent of the women patients.

It is evident that multiple primary malignancy, of the large bowel at least, is not a rare or even an unusual phenomenon. Any patient with a carcinoma of the rectum or the colon has an increased risk of developing other sites of cancer, simultaneously or at different time intervals. The relative frequency of primary polycancers may be high or low, depending upon the author; but the fact that

it is a definite possibility is the important point. All physicians must be alert to this possibility and must abide by the following rules when a cancer patient is dealt with:

1. Preoperative investigations should include a careful physical examination, proctosigmoidoscopy, and roentgenologic examinations. In men, upper gastrointestinal roentgenograms are advisable. The slightest gastrointestinal symptom in women should warrant barium meal studies.

2. During surgery meticulous exploration of the colon and of all abdominal organs should be performed. Coloscopy often reveals lesions missed by palpation.

3. After surgery patients should be checked at regular intervals, both clinically and radiologically. Each should remain on the cancer detection list and be considered a candidate for an additional primary cancer even though he has achieved a survival time which makes him theoretically a surgical cure, whether it be 5, 10, or even 20 years.

REFERENCES

1. Bacon, H. E., and Tavenner, M. C.: Multiple Primary Malignant Tumors Involving the Colon and Rectum, Am. J. Surg. **83**: 1-55, 1952.
2. Billroth, H.: Die allgemeine Chirurgie, Pathologie u. Therapie, Berlin, 1889, R. Reimer, p. 908.
3. Brindley, G. V., and Rice, J. S., Jr.: Multiple Primary Malignancies of Large Intestine, S. Clin. North America **32**: 1499, 1952.
4. Cramer, W.: On an Antagonism in the Development of Malignancy in Two Different Organs, J. Path. & Bact. **43**: 77, 1936.
5. Dukes, C. E.: The Hereditary Factor in Polyposis Intestini or Multiple Adenomata, Cancer Rev. **5**: 241, 1930.
6. Ginsburg, L., and Dreiling, D. A.: Successive Independent (Metachronous) Carcinomas of the Colon, Ann. Surg. **143**: 1, 1956.
7. Hanlon, F. R.: Multiple Primary Carcinoma, Am. J. Cancer **15**: 2001, 1931.
8. Hurt, H. H., and Broders A. C.: Multiple Primary Malignant Neoplasms, J. Lab. & Clin. Med. **18**: 765, 1933.
9. Lockhart-Mummery, J. P., and Dukes, C. E.: Familial Adenomatosis of the Colon and Rectum; Relationships to Cancer, Lancet **2**: 586, 1939.
10. Long, J. W., Mayo, C. W., Dockerty, M. B., and Judd, E. S., Jr.: Recurrent Versus New and Independent Carcinomas of the Colon and Rectum, Proc. Staff Meet., Mayo Clin. **25**: 169, 1950.
11. Mercanton, F.: Des carcinomas primaires multiples, These de Lausanne, 1893, Rev. med. de la Suisse Rom. **13**: 173, 1893.
12. Mider, G. B., Schilling, J. A., Donovan, J. C., and Rendall, E. S.: Multiple Cancer, Cancer **5**: 6, 1952.
13. Muller, R. F.: Ueber multiple Nichtystematisierte primare Carcinome und ihre Haufigkeit, Ztschr. Krebsforsch. **31**: 339, 1930.
14. Owen, L. J.: Multiple Malignant Neoplasms, J. A. M. A. **76**: 1329, 1921.
15. Stalker, L. K., Phillips, R. B., and Pemberton, J. de J.: Multiple Malignant Lesions, Surg., Gynec. & Obst. **68**: 595, 1939.
16. Stenstrom, J. D., and Ford, H. S.: Carcinoma of the Colon; Analysis of 1,000 Cases With Particular Reference to Polyps and Multiple Carcinoma, Am. J. Surg. **88**: 1, 1954.
17. Ward, R.: Radium Treatment of Epitheliomata of the Skin, Brit. M. J. **2**: 511, 1930.
18. Warren, S., and Ehrenreich, T.: Multiple Primary Malignant Tumors and Susceptibility to Cancer, Cancer Research **4**: 554, 1944.
19. Warren, S., and Gates, O.: Multiple Primary Malignant Tumors, Am. J. Cancer **16**: 1358, 1932.

REGIONAL ENTERITIS IN A LARGE GENERAL HOSPITAL

With an Analysis of Twenty-Nine Cases in Negroes

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IF THERE is any excuse for another contribution to the already far-ranging literature of regional enteritis, it is that at present almost no attention seems to have been paid to this disease as it occurs in the Negro race. This is true even in contributions from the South, which is curious, for disease in the Negro has always been a matter of concern to Southern physicians. It was necessarily their concern in slavery days, and it is still their concern because of the large concentrations of Negroes in many Southern states, of which Louisiana is one.

From slavery days on, the belief has persisted, no matter what the biologists may think, that some diseases, at least, differ in the Negro and white races. Some of the early literature, such as the report of Dr. S. A. Cartwright[2] in 1851, is incredibly unscientific, even in the light of the limited medical knowledge then available. The report of the late Dr. Rudolph Matas[10] on surgical diseases in the Negro, which was published in 1896, is, on the contrary, still a medical classic. Much that is in it, in spite of the advances made during the past 60 years, would still be subscribed to by those of us who practice at Charity Hospital of Louisiana at New Orleans, from which Dr. Matas' data were secured.

Regional enteritis was not a recognized clinical entity when Dr. Matas' report was published, and it does not appear in the extensive study on racial trends in surgical diseases published by the late Dr. Urban Maes,[7] also from the New Orleans Charity Hospital, in 1936. This is understandable, since his statistics end with the decennium ending in 1934.

INCIDENCE

The single article in the literature specifically devoted to regional enteritis in the Negro was published by Marks and Fink,[8] in 1949, from Harlem Hospital in New York, in which the population is predominantly Negro but in which only 4 cases, one fatal, were observed between 1936 and 1948. In a review of the 299 articles published between 1932, when the first description of Crohn's disease appeared,[3] and the date of their publication, the authors were able to find only 26 case histories of regional enteritis in the Negro.

As they pointed out, very few articles on the subject mention race. They might have added that reviews of the literature of regional enteritis are frequently difficult for another reason; serial reports are cumulative and case reports are often published more than once. As a result, if the authorship or

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origin of the contribution, or both, are not recognized, some cases are likely to be counted more than once. My own review of the literature since Marks and Fink's article was published is open to this error.

My review, which is comprehensive but not entirely inclusive, covers 116 articles, in which 3,487 cases of regional enteritis are reported. These cases range from single case reports and reports of small groups of cases to the large series reported by Marshak and Wolf[9] in 1955 from Mount Sinai Hospital in New York and by Van Patter and his associates[11] in 1954 from the Mayo Clinic.

In 2,647 of these cases the race was not stated, and in the remaining 840 cases only 25 cases were specifically mentioned as occurring in the Negro. Included in this number are the 21 cases in the Negro reported, without special comment, by Loria,[6] in 1949, from the New Orleans Charity Hospital. The presumption thus seems warranted that regional enteritis is indeed an uncommon disease in the Negro.

The 29 cases in the Negro which I am now reporting (Fig. 1) occurred in a total of 54 cases of regional enteritis treated at the New Orleans Charity Hospital between July 1, 1937, when the present record system was instituted, and Sept. 1, 1957. Twenty-eight of the 54 cases, including 13 of the 29 Negro cases, were observed during or after 1950.

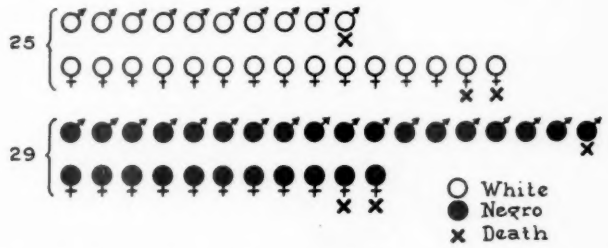

Fig. 1.—Distribution according to race and sex of 54 cases of regional enteritis observed at Charity Hospital of Louisiana at New Orleans.

These 54 cases were selected from the 300-odd records of enteritis which were examined. All 54 were proved irrefutably, one by post-mortem examination, 6 by roentgenologic evidence, and 47 by surgery. A number of other case records examined were probably instances of regional enteritis, but the evidence was entirely clinical and was not regarded as sufficiently convincing to warrant their inclusion. Among its other characteristics, regional enteritis is a highly deceptive disease.

A survey of the hospital records before 1937 undoubtedly would have revealed additional cases of regional enteritis, most of them probably not correctly identified. I remember witnessing an operation on a Negro woman in the fall of 1933 for disease of the terminal ileum and cecum which, in the light of later knowledge, I am certain was regional enteritis although none of us present realized it.

At any rate, regional enteritis is apparently a disease of such infrequency in a hospital population now in the neighborhood of 70,000 yearly, with a Negro component approaching 70 per cent, that any discussion of its incidence in either race would be entirely academic.

Regional enteritis reveals no marked predilection for either sex. In the small number of cases which make up this series, it is therefore probably of no significance that there were more white women than white men and more Negro men than Negro women (Fig. 1).

AGE

The age span in regional enteritis is wide, and so it was in this series (Fig. 2), from 8 years in the white and 13 years in the Negro at one extreme to 77 years for both races at the other extreme. The number of cases in older persons is, however, rather striking. Seven white cases and 5 Negro cases occurred in persons 50 years of age and older, and 4 of these (2 white and 2 Negro) occurred in patients between 71 and 77 years of age.

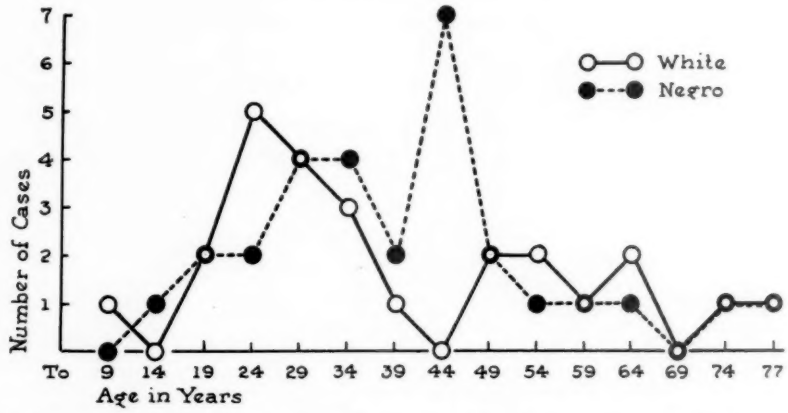

Fig. 2.—Distribution according to race and age of 54 cases of regional enteritis.

So large a proportion of cases in older patients is not at all usual. Last year, when a certain famous patient was operated upon for regional enteritis and anti-administration columnists and commentators began to quote, selectively, from a small monograph which I had recently written on the disease,[1] one of the broadcasting companies courteously afforded me the opportunity for more correct quotation.

In many of the 170 articles which I reviewed before preparing a statement, age, like race, was not mentioned, or it was merely stated that the age incidence followed the usual pattern of concentration in the middle adult years. Only 7 of 60 reports of individual cases or of 2 or 3 cases were concerned with patients 50 years of age and older. Twenty-two articles dealt with series of cases in which the age range was stated, but in only 5 of the series were there any patients 60 years of age and older. The 990 cases analyzed in these 22 articles included the 603 cases reported by Van Patter and his associates[11] from the Mayo Clinic. Only 10 patients in this series were between 61 and 74 years of age. The 2 oldest patients in the 30 Negro cases collected or reported by Marks and Fink[8] were both 58 years of age.*

*The single case report in these 170 articles which fitted the age group and surgical status of the patient who was causing the columnists and commentators such concern was included in the 40 cases studied from Billings Hospital in Chicago by Dashiell and his associates[4] in 1951. The parallel was quite precise; the patient, a 64-year-old man, underwent ileotransverse colostomy. Except for a single apparent recurrence, lasting one day, which occurred 5 months after operation, he was well at the end of 9 years.

In view of the data in the literature, the large proportion of older patients in this small series, about 22 per cent, seems to prove that it is not always true that the disease becomes spontaneously milder and burns itself out in older patients. It may or may not be significant that 9 of the 12 in this group were encountered in the last 7 years. Apparently, as the life span increases, regional enteritis, like other diseases once regarded as predominantly diseases of younger persons, will be encountered more often in our aging population.

There was no particular difference in the manifestations of the disease in the older age group. Some of them had very stormy courses and some of them responded to treatment and tolerated extensive surgery quite as well as younger persons.

There were 3 deaths in the 12 patients 50 years of age and older. A 77-year-old Negro woman was admitted moribund, in uremic coma. Autopsy revealed cardiorenal disease and regional enteritis; she had had symptoms of the intestinal disease but it played only a minor role, if any, in her death. A 61-year-old white woman, a hypertensive patient with cardiac disease, died of mesenteric vascular occlusion 9 days after a simple exploration. A 71-year-old white man, a cardiac patient with massive ascites, died after dehiscence of the surgical wound; he had undergone resection of the ileum, which was the site of a perforation, which had given rise to a pelvic abscess.

All three of these fatal cases do point up one fact—that diagnosis may be more difficult and the surgical risk greater in older persons because of the existence of systemic complications. A young Negro man in this series had both malaria and pleurisy when he presented himself in his first attack of regional enteritis, and 3 young white women had pelvic inflammatory disease. The remaining complications, which included hypertension, cardiac disease, cardiorenal disease, diabetes, portal cirrhosis, and diverticulosis, all occurred in older patients. There was no significant racial difference in their distribution.

PATHOLOGIC PROCESS

The pathologic process was essentially the same in both races. In both it included ulcerative and obstructive disease. The ileum was affected in all 54 cases. The cecum was additionally involved in 4 white and 5 Negro patients, the jejunum in 1 white and 2 Negro patients, the cecum and ascending colon in 1 white patient, and the ileocecal valve in 1 Negro patient. Skipped areas were present in 4 white and 4 Negro patients, and 2 of the 5 perforations occurred in Negroes. One Negro patient had an ileocolic intussusception. These findings and their proportions conform, in general, to the observations made in 750 cases recently studied from Mount Sinai Hospital in New York by Marshak and Wolf.[9]

In view of the statement in Marks and Fink's[8] article that no instance of fistulous disease had been found in Negro patients, it is worth mentioning that 2 of the 7 fistulas in the Charity Hospital series occurred in this race.

CASE REPORTS

CASE 1.—One patient, a 60-year-old Negro man, developed an internal fistula after resection, at the site of the anastomosis. It was successfully resected, together with an external fecal fistula. When an incisional hernia was repaired in May, 1957, 4 years after the last operation, he had no complaints and had gained weight.

CASE 2.—Of even more interest is the 52-year-old Negro woman who underwent a short-circuiting operation followed by resection. Three years after the second operation, roentgenograms showed a number of communications between the small bowel and the greater curvature of the stomach near the pylorus, as well as a single communication between the stomach and the transverse colon. The fistulous areas were resected, after which a small fecal fistula appeared. The patient then disappeared for 18 months. When she reappeared, the fistula had closed spontaneously, she had gained weight, and she had no complaints except some increased frequency of bowel movements.

CLINICAL PICTURE AND DIAGNOSIS

There was little of convincing etiologic value in any of these histories. A white patient traced the onset of her symptoms to her father's suicide, and a Negro traced his to the receipt of a notice to report for induction into military service. Another Negro man had a not very convincing history of trauma and a third related his symptoms to an emergency operation for incarcerated hernia a month before.

Most of these patients presented, more or less completely, what has come to be regarded as the classical picture of regional enteritis, with abdominal pain as the outstanding feature. Weight loss was notable and often occurred over an incredibly short time. It ranged from 15 to 65 pounds in white patients and from 10 to 30 pounds in Negroes; a white woman was said to have lost 50 pounds in 3 months. In view of the extreme emaciation presented by many of these patients—one weighed only 65 pounds—it is a tribute to the nursing care which they received that only one of them, a Negro woman, developed a decubitus ulcer.

In retrospective examination of the histories, the diagnosis usually seemed clear-cut, which is a very different matter, of course, from making it at the moment it is needed. There were 24 separate diagnostic possibilities considered in these 54 cases, with obstruction (12) the most frequent and appendicitis (10) the second most frequent. Appendicitis would probably have been the most frequent except that 9 patients had already had their appendices removed, 3 in connection with the present illness and 6 too long before to bear any relation to it.

In 26 cases, 14 in white patients and 12 in Negroes, there was no history of diarrhea. Six of the 9 appendectomies in white patients and 5 of the 6 appendectomies in Negroes occurred in patients who did not have diarrhea. This is an interesting observation, in view of the belief, which sometimes leads to tragic error, that a patient with diarrhea is unlikely to have acute appendicitis. One cannot blame most of the surgeons who performed these emergency operations in the preoperative belief that the diagnosis was acute appendicitis. This is particularly true of the 4 cases, 2 in Negroes and 2 in white patients, in which purgatives had been taken. One does not delay surgery when a purgative has been taken if acute appendicitis is in question.

A number of patients had symptoms of obstruction, which did not prove complete in any instance, although in several cases the caliber of the bowel was so reduced that complete obstruction would have been a matter of time. In one white woman the diagnosis was complicated by urinary symptoms, which were readily explained when the ureter was found adherent to the affected intestine at operation; a fistulous connection would undoubtedly have resulted if operation had been deferred.

MANAGEMENT

Generally speaking, in cases of considerable duration, the white patient was more likely to have had previous treatment than the Negro. Three white patients had undergone appendectomy, one with incision and drainage of a presumed appendiceal abscess, before admission, and another had had an incision and drainage of an abscess of undetermined etiology. In none of these cases was there anything to indicate that the patients were being treated with either realization or suspicion of the correct diagnosis.

The management of regional enteritis depends upon a number of considerations, including the stage and duration of the disease, the status of the patient, and the clinical judgment and experience of the surgeon. Other considerations also cannot be ignored in a public hospital. One is the cooperation of the patients, and here some racial differences seem to be evident. All 6 of the patients in whom the diagnosis was made by x-ray evidence alone were requested to return for further investigation, for a further trial of conservative therapy, or, in one or two instances, for surgery. None of them accepted the advice. Five of the 6 patients in this group were Negroes, many of whom are still inclined to take illness rather lightly when it does not trouble them at the moment. Another Negro patient who had undergone only appendectomy was advised to submit to resection but declined and had not returned. In view of the good short-term results apparent in a few of these cases after appendectomy alone, it may be that his judgment was as good as the surgeon's.

In 12 white and 14 Negro patients the duration of the disease was from 12 hours to one month, and the condition was acute in the sense that there had been no previous attacks. There was little really precipitate surgery, either in this group or in the other cases in the series. Whenever it was practical, the patients were given a trial of conservative therapy or had already had such treatment outside of the hospital.

When, however, one is dealing with patients in a public hospital, certain hard social and economic facts must also be taken into consideration. One is that such patients often cannot afford, or will not follow, a regimen of medical management. Another is that they will not return regularly for observation, particularly when they begin to improve. Negroes were somewhat more casual than white patients about returning for observation after surgery. The third consideration is that patients in this economic stratum cannot afford to be invalids.

Hospital charts bear none of these reasons for prompt surgery, but I have no doubt that in some of these cases, at least, these considerations weighted

the scale in favor of surgery which might otherwise have been deferred in favor of a longer trial of conservative measures.

The number of operations (47) is too small to permit delineation of a surgical pattern (Fig. 3). I find it interesting, however, that 11 of the 15 appendectomies were performed before 1944 and that up to this time, only one of the 6 explorations and only 5 of the 16 resections in the series had been performed. These data are in line with 2 present-day concepts: (1) if the abdomen is opened on the incorrect diagnosis of acute appendicitis, the best plan is to limit the procedure to exploration, and (2) if surgery is undertaken electively, resection is the procedure of choice, with short-circuiting reserved for cases in which there is some specific reason, such as acute obstruction or active infection, not to perform resection primarily.

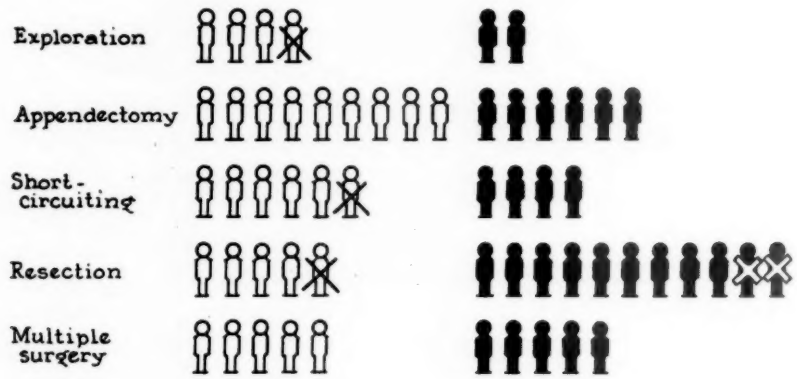

Fig. 3.—Distribution according to age, surgical management, and mortality (X) of 47 cases of regional enteritis.

RESULTS

If anything, the Negro tolerated surgery better than the Caucasian. There were 3 deaths in the 25 operations in white patients, against 2 in the 23 operations in Negroes (Fig. 3). I doubt that either of the Negro deaths would have occurred today.

The first of these deaths was in a 42-year-old woman, with obstructive symptoms for a week. She tolerated resection well but died of bronchopneumonia on the third day. This was in 1939; today, penicillin would probably have saved her.

The second Negro death occurred in a 26-year-old man with 10 skip lesions, several of them partially obstructive, in the ileum. After 4 segmental resections had been done, the abdomen was closed, with the intention of caring for the other lesions similarly at a second operation. Evisceration occurred on the seventh day and the patient died 3 days later. This was in 1944. I doubt that segmental resections for skip areas would be performed today. We know now that large portions of the small bowel can be removed with impunity under antibiotic protection and that troublesome residua can usually be controlled satisfactorily by medical measures.

Two surgical deaths in white patients, one from mesenteric vascular occlusion and the other after evisceration, have already been mentioned. A third occurred in a 33-year-old woman who had a recurrence of the symptoms

of her 2-year-old disease 3 weeks postpartal. She tolerated short-circuiting with exclusion without difficulty but died suddenly 24 hours later, possibly from coronary occlusion, more probably from pulmonary embolism; autopsy was not permitted. Postpartal recurrence is not at all uncommon in patients with regional enteritis and is likely to be serious even when, as in this case, the pregnancy has proceeded uneventfully.

There were no deaths in the 10 instances of multiple surgery in this series. Four of the 5 white patients and 3 of the 5 Negro patients in this group were under 40 years of age. In 3 patients, one a Negro, resection was done promptly after short-circuiting, as part of the plan of management.

There is no formal follow-up system at the New Orleans Charity Hospital, and patients who do not return for continued observation as directed are simply lost to view. Most of the other survivors of surgery either did not pay any subsequent visits to the clinic or were observed for such short periods, usually only a few weeks, that no statements can be made about end results.

Two patients are known to have died, each 2 years after operation, which in one instance, in a Negro patient, was an appendectomy and in the other, in a white woman, was a short-circuiting operation. Whether the disease played any part in the outcome is not known; in neither instance was the pathologic process severe.

At present there are 5 known recurrences, one in a Negro after exploration and 4 in white patients, 2 after appendectomy and 2 after resection.

TABLE I. SHORT-TERM RESULTS OF SURGERY IN 11 PATIENTS WITH REGIONAL ENTERITIS AT CHARITY HOSPITAL OF LOUISIANA AT NEW ORLEANS

CASE NUMBER	RACE SEX	AGE	PRIMARY PROCEDURE	POSTOPERATIVE OBSERVATION (YEARS)	RESULTS
42	WF	37	Resection	2¾	Excellent, after recovery from 6 postoperative abscesses
11	NF	26	Resection	5	Excellent
25	NM	44	Resection	2½	Excellent
29	NM	60	Resection	4	Good, after secondary resection; exploration; excision of fistula at site of anastomosis and fecal fistula; and late incisional herniorrhaphy
40	WF	33	Short-circuiting	3	Able to work
38	WF	63	Short-circuiting	6	Excellent, cardiac and diabetic status improved
20	NM	71	Short-circuiting	2	Excellent, cardiac and hepatic status improved
48	WM	45	Exploration	4	No symptoms, interim cholecystectomy
14	NM	47	Exploration	4	No symptoms
35	WF	15	Appendectomy	2¾	No symptoms
47	WM	20	Appendectomy	11	No symptoms

In 11 patients (Table I) the period of postoperative observation covered 2 to 11 years, the follow-up evaluations frequently being possible only because the patients returned to the hospital or the clinic for other conditions. The results in these 11 cases were all good, either absolutely or by the criteria laid down by Dyson, Hodes, and Rhoads,[5] that a patient may be considered to have a good result if he is performing his daily duties without periods of hospitalization or prolonged periods of pain, fever, or discomfort, if he is gaining weight, and if his bowel function is normal or he is suffering from only mild diarrhea.

By these standards, or even more strict ones, the majority of these patients were in good condition when last seen, although I am well aware that the longer the period of observation, the poorer the end results are likely to be. These patients, however, consider themselves well, and that is a very important consideration indeed. Two of the patients (Cases 25 and 40) had increased frequency of stools, but the diarrhea was not incapacitating and they were gaining weight despite it. One or two patients had roentgenologic evidence of persistent or recurrent disease, but it was not giving rise to symptoms and their surgeons, wisely, did not regard it as an indication for further surgery. Some of these patients had stormy postoperative courses, and one (Case 29) required multiple surgery before he reached his present level of improvement.

A 71-year-old man (Case 20) was a poor surgical risk because of serious cardiac disease and cirrhosis of the liver. At the end of 2 years, he has no symptoms referable to regional enteritis and his cardiac and hepatic status are both greatly improved; he continues under observation because of these conditions. A 63-year-old white woman (Case 38), well 6 years after a short-circuiting operation, continues under observation as a psychotic problem. A 45-year-old white man (Case 48) now has only orthopedic problems.

Perhaps the most remarkable patient in the list is a 26-year-old Negro woman (Case 11) who had 5 children within 5 years after resection and had no symptoms referable to the intestinal disease during the entire obstetric experience; her only difficulty, in fact, was mild pre-eclampsia, readily controlled, in the fifth pregnancy. She is living proof of the fact, evident in several case reports and series in the literature, that pregnancy may have the same beneficial effect in regional enteritis that it is known to have in several other diseases.

In many respects, the most interesting feature of the good results, short-term though they be, in these 11 cases is the fact that they were secured, or, more correctly, that they occurred, after all varieties of surgery, including appendectomy and simple exploration, which obviously could have no effect upon the enteric disease. These latter operations were all done in instances of acute disease, and the results seem to prove the point made by Dyson and his associates[5] that the chances of spontaneous resolution in acute regional enteritis without fibrosis are "not inconsiderable." Be this as it may, a survey of the procedures and results in these 11 patients gives the surgeon no mandate to speak dogmatically about the management of regional enteritis.

SUMMARY

This is a somewhat negative report, amounting to little more than the fact that regional enteritis is not a frequent disease in either the Negro or the white race and that it is apparently much less frequent in Negroes than in Caucasians. The older age incidence of this disease seems to be increasing in both races.

The manifestations of regional enteritis and the response to therapy seem about the same in both races. Good results may occur after all varieties of therapy, including procedures such as appendectomy and exploration, which obviously do not affect the enteric disease.

These remarks are based upon a study of 29 Negro and 25 white patients observed during the last 20 years at Charity Hospital of Louisiana at New Orleans. The chief value of the analysis is, perhaps, that it was carried out in an institution in which there is the largest concentration of Negro patients in any hospital in the country and that the study was, in a sense, controlled, in that white and Negro patients were treated in the same circumstances by the same visiting and resident hospital staffs.

REFERENCES

1. Boyce, F. F.: Regional Enteritis. Diagnostic and Therapeutic Considerations, Philadelphia and Montreal, 1955, J. B. Lippincott Company.
2. Cartwright, S. A.: Report on the Diseases and Physical Peculiarities of the Negro Race, New Orleans M. & S. J. **7**: 89, 1851.
3. Crohn, B. B., Ginzburg, L., and Oppenheimer, G. D.: Regional Ileitis. A Pathological and Clinical Entity, J. A. M. A. **99**: 1323, 1932.
4. Dashiell, G. F., Kirsner, J. B., Klotz, A. P., and Palmer, W. L.: Regional Enteritis. A Follow-Up Study of Forty Cases, M. Clin. North America **35**: 227, 1951.
5. Dyson, W. L., Hodes, P. J., and Rhoads, J. E.: Late Results in the Surgical Treatment of Regional Enteritis, Pennsylvania M. J. **57**: 433, 1954.
6. Loria, F. L.: Regional Enteritis, South. Surgeon **14**: 542, 1949.
7. Maes, U., and McFetridge, E. M.: Racial Trends of the Negro and White in Certain Surgical Diseases, Am. J. Surg. **33** (n. s.): 5 and 20, 1936.
8. Marks, J. A., and Fink, S.: Regional Enteritis in the Negro, Rev. Gastroenterol. **16**: 623, 1949.
9. Marshak, R. H., and Wolf, B. S.: Roentgen Findings in Regional Enteritis, Am. J. Roentgenol. **74**: 1000, 1955.
10. Matas, R.: The Surgical Peculiarities of the American Negro, Tr. Am. S. A. **14**: 1, 1896.
11. Van Patter, W. N., Bargen, J. A., Dockerty, M. B., Feldman, W. H., Mayo, C. W., and Waugh, J. M.: Regional Enteritis, Gastroenterology **26**: 347, 1954.

A METHOD OF IDENTIFICATION OF INTESTINAL BLEEDING EXPERIMENTALLY PRODUCED IN DOGS

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ONE of the most challenging problems to the general surgeon is the management of the patient with massive gastrointestinal bleeding of undetermined origin.[1, 6] Gastrointestinal hemorrhage which arises from the esophagus, stomach duodenum, distal colon, rectum, or anus can be localized by x-ray examination of the gastrointestinal tract, esophageal balloon tamponade, or sigmoidoscopic examination.[2, 4, 5] When these sites of gastrointestinal bleeding have been eliminated, other parts of the intestinal tract, that is the small bowel or proximal colon, must be investigated. When a positive diagnosis cannot be established during the preoperative investigation of a patient with massive bleeding, exploratory laparotomy may become necessary, at which time, localization of the bleeding point may still be a problem.[1, 3]

The experimental method presented in this paper was devised in an effort to help the surgeon establish the site of gastrointestinal bleeding in patients who come to surgery for massive hemorrhage where other studies are inadequate or inaccurate. The experimental technique consists of the injection of radioactive iodinated human serum albumen (RISA) into the mesenteric arterial bed followed by detection of radioactivity along the small bowel or colon. This method is preferred to the systemic intravenous route of injection because the radioactivity is thus concentrated in the vascular bed supplying the bleeding site. This technique was studied in a series of dogs in whom intestinal bleeding points were constructed experimentally.

METHOD

Dogs were anesthetized with intravenous pentobarbital sodium and a midline incision was made from the epigastrium to the lower abdomen. The intestine was delivered into the wound. A 0.5 cm. incision was made in the bowel on its mesenteric border. A vasa rectus was temporarily occluded with a Potts bulldog clamp 1 cm. from the intestine and the distal cut end was ligated. The proximal cut end of the vessel was inserted into the incision in the bowel and a preplaced purse-string suture was lightly tied as the clamp occluding the vessel was removed (Fig. 1). This established an intraluminal arterial bleeding point.

The abdominal aorta was exposed and a Potts clamp was applied above the trifurcation. Ten to 20 microcuries of RISA in 1 to 10 c.c. of normal saline

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was injected into the aorta above the clamp using a 22-gauge needle (Fig. 2). The Potts clamp was left on the aorta for 5 to 10 minutes after the injection. Digital compression of the aorta is simpler than clamping and requires no dissection. It is equally satisfactory. The level of radiation received by the operator's hand is well below safe levels.

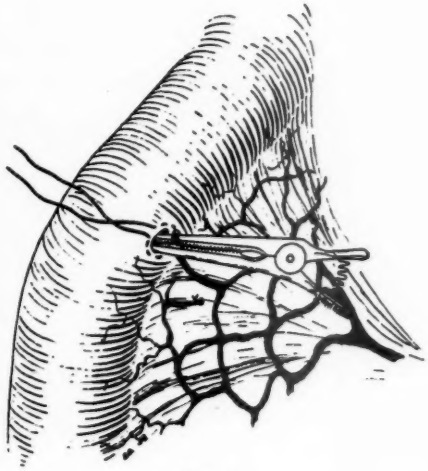

Fig. 1.

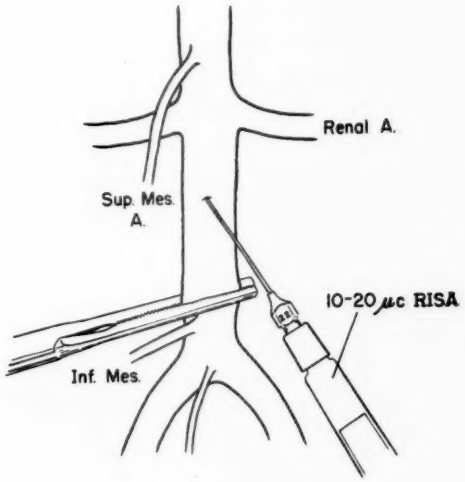

Fig. 2.

Fig. 1.—Construction of arterial bleeding point.
Fig. 2.—Intra-arterial injection of RISA into aorta.

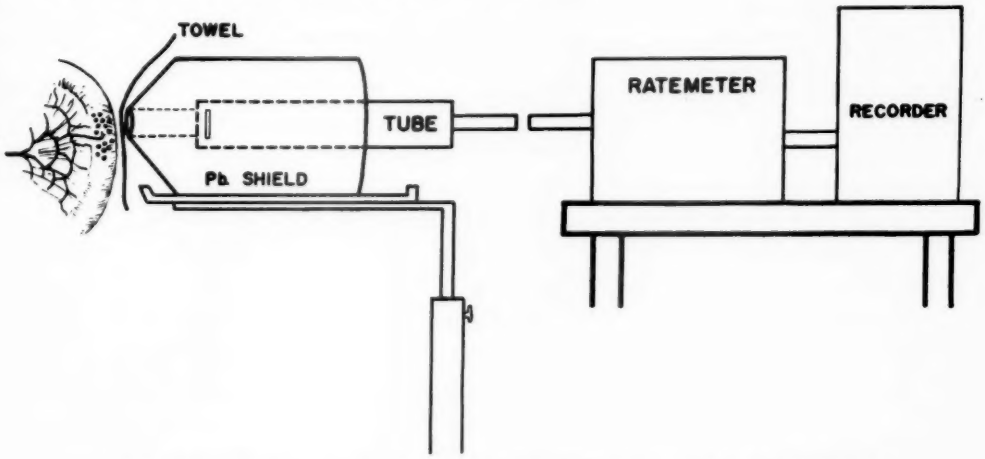

Fig. 3.—Schematic arrangement for detection of experimental bleeding point.

A scintillation counter was used as a detection device to identify the levels of activity in various portions of the intestine (Fig. 3). Lead shielding (1¾ inches) was used around and in front of the scintillation crystal. A 2 cm. aperture was used to decrease background activity in the room and obtain directionality of counting. The scintillation tube was connected to a precision rate meter which determined the level of activity measured in counts per minute. The results were recorded with an Esterline-Angus recorder. The scintillation tube was mounted in a horizontal plane on a Mayo stand, opposite the operator, directed across the dog's abdomen, and covered with a sterile drape.

Immediately after injection of the radioactive substance the small bowel or colon was systematically passed closely across the aperture of the columnated scintillation tube. Levels of activity were determined over areas of uninvolved bowel and over the areas of experimentally established bleeding. Results were considered significant when the counting rate over the bleeding point was twice animal background activity or greater.

One to 7 bleeding points were constructed in each of 6 dogs to study the effects of different volumes and concentrations of radioactivity, methods of injection, and the accuracy of bleeding-point identification. More than one intra-arterial injection was given to 2 animals to establish reproducibility and to determine the accuracy of the method in detecting bleeding points against elevated background activity.

RESULTS

Six dogs were used in this study and 21 arterial bleeding points were constructed. After the intra-aortic injection of RISA in the presence of active intestinal bleeding, a characteristic curve was obtained (Fig. 4). Prior to injection, animal and room background activity was approximately 50 counts per minute (cpm). After injection of 10 or 20 microcuries of RISA, the animal background activity over the uninvolved bowel ranged from 100 to 300 cpm. When the area of active bleeding was encountered, radioactivity levels ranged from 400 to 1,000 cpm.

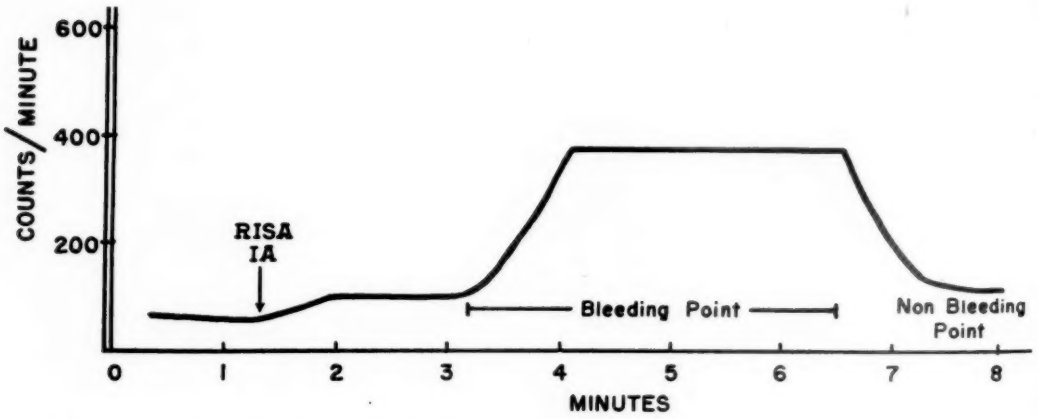

Fig. 4.—Typical curve after intra-aortic injection of RISA over experimentally produced bleeding points and nonbleeding points.

Of the 21 bleeding points constructed in 6 dogs, 8 had levels of activity of 3 times background or greater, 8 bleeding points had levels of activity between two and three times background, and only one had activity less than twice background (Table I). Four others did not demonstrate a significant rise in activity at the prepared site of bleeding. Examination of these last 4 areas showed that bleeding had ceased prior to the injection of the radioactive substance. Study of the 21 bleeding points produced significant positive or negative results over 20 bleeding points and nonsignificant results in one.

TABLE I. IDENTIFICATION OF BLEEDING POINTS EXPERIMENTALLY PRODUCED USING RISA IN DOGS

DOG	BLEEDING POINT NUMBER	DOSE (μC)	VOLUME (C.C.)	INCREASED ACTIVITY (TIMES BACKGROUND)	RESULT
I	1	20	1	3	Excellent
II	18.2	10	10	0	No bleeding
	3			2	Good
	4	20	8	2	Good
III	18.2	20	2	0	No bleeding
	3			1	Fair
	4			3	Excellent
IV	1-5	10	10	2	Good
	6	20	2.5	3	Excellent
	7			2	Good
V	18.2	20	5	3	Excellent
VI	1-3	20	5	3	Excellent

Determinations were made using 10 or 20 microcuries of radioactive iodinated human serum albumen (RISA) in 10 to 20 c.c. of normal saline. Best results with active bleeding points were obtained using 20 microcuries of RISA in 1 to 5 c.c. of solution. This dosage gave levels of activity of three times background or greater in 7 of 8 instances. When 10 microcuries of RISA and/or larger volumes of solution (8 to 10 c.c.) were used, radioactivity over the bleeding point was between two and three times background in 7 of 9 instances. Bleeding points can be identified with this lower dosage of radioactivity but the results are less reliable. With these experiments, 20 microcuries was the lowest dosage producing consistently satisfactory results and it was also apparent that the volume of solution injected is a critical factor.

The appearance of radioactivity in the intestine after intra-aortic injection of the isotope could be detected very readily. Significant levels of activity were produced in 30 to 60 seconds over or within 3 cm. of 11 of the 12 bleeding points constructed. The area of active bleeding could thus be well localized when the dosage, volume, and circumstances were optimal. An attempt was made to construct venous bleeding points but a satisfactory preparation could not be constructed. However, 4 venous bleeding points were constructed and nonsignificant rises in activity were obtained.

In this series, there was no gross evidence of bleeding such as discoloration or distention of the bowel but the presence of bleeding could be detected by means of the radioactive tracer which was uniformly identified in the area of the bleeding point. In one animal, the bleeding point was constructed and sufficient time was permitted for the intestinal tract to be filled and discolored with blood. The site of bleeding nonetheless could be identified by this method quite easily. In another instance 2 feet of small bowel became filled with radioactive blood making it difficult to localize the exact point of bleeding. To resolve this problem the blood was expressed into a segment of uninvolved bowel and time was permitted for reaccumulation of circulating active blood at the bleeding

point. Ten to 15 minutes later, evidence of bleeding could be clearly demonstrated within a 2 to 4 cm. segment of bowel by passing it before the scintillation detector.

In one animal 10 microcuries of RISA was injected into the saphenous vein to test the efficacy of this route of administration in identification of a site of bleeding. Levels of activity increased slowly at the bleeding point over 5 to 10 minutes. These were maximally only twice, or less than twice, animal background activity. These results were not considered satisfactory. The scintillation counter was directed over the abdomen of the animal in its 4 quadrants and much of the activity was found in areas of the liver, spleen, and stomach.

DISCUSSION

For the unusual case of active intestinal bleeding in which meticulous diagnostic studies have failed to disclose a lesion, exploratory laparotomy may become necessary. If the lesion is not found by inspection and palpation of the bowel at the time of surgery, this method, experimentally evolved in dogs, may be of value in identifying the site of hemorrhage.

Radioactive iodinated human serum albumen was used in this study because it is readily available in hospitals using radioactive isotopes, safe to work with, emits both beta and gamma particles, and can be detected in low levels of activity. Other isotopes, such as radioactive chromium and phosphorus, could be used to tag red cells, but these methods are more time-consuming and less readily available. These isotopes were not investigated in this series. A scintillation counter was used to detect gamma and beta radiation penetrating the intestinal wall. Lead shielding about and in front of the scintillation crystal was used to decrease room background counting rates, obtain directionality of detectable beta radiation, and thereby minimize the amount of isotope administered.

The injection of a radioactive isotope directly into the arterial bed of an active bleeding point delivers the tracer substance to the origin of bleeding where it pools immediately. Temporary aortic occlusion, with a Potts clamp or by manual compression, permits controlled injection into the aorta so that the indicator does not run off to the extremities but enters the mesenteric arterial bed. Intravenous injections of RISA are associated with gradual and smaller increases in activity at the bleeding point because dilution of the isotope in the circulating blood volume does not permit high concentrations of activity to be pooled at the bleeding site. To accomplish this, large doses of of radioactivity would have to be used which raise the animal background activity so that differences in activity over bleeding and nonbleeding sites would be less significant.

The volume of solution optimal for accurate results with the intraaortic route of injection will vary with the volume necessary to fill the aorta from the point of occlusion to the superior or inferior mesenteric artery. The dose of activity given to the subject will depend upon the thickness of the bowel through which the isotope must penetrate to be recorded, the characteristics of the particles emitted, and the efficiency and type of counting device used. Using the

technique described, immediate and satisfactory positive or negative results were obtained in the dog using 20 microcuries of RISA in 1 to 5 c.c. of solution with temporary aortic occlusion in 20 of 21 bleeding points. This technique permits identification of a bleeding site when no visible evidence of blood in the bowel is observed or when the small intestine and colon are completely filled with blood.

The experimental technique described of occluding the aorta with a Potts clamp may be used in patients but digital compression of the aorta at its bifurcation by the surgeon is simpler and produces satisfactory and safe occlusion. Injection of the radioactive isotope with a 22-gauge needle is not associated with significant bleeding from the aorta.

The method might be adapted to include use of a small end window Geiger-Mueller probe counter columnated to demonstrate bleeding in the esophagus, stomach, duodenum, or rectosigmoid using P^{32}-tagged red cells. These methods have not been investigated in this series.

SUMMARY AND CONCLUSIONS

1. A method of identification of intestinal bleeding points, experimentally produced in the small bowel and colon of dogs, has been described.

2. Twenty-one bleeding points were produced in 6 dogs and 10 to 20 microcuries of RISA in 1 to 10 c.c. of normal saline was injected into the aorta above a Potts clamp applied at the level of the bifurcation.

3. Levels of activity were detected by passing the small bowel or colon across the columnated aperture of a shielded scintillation counter connected to a precision rate meter recording the results with an Esterline-Angus recorder.

4. Significant positive or negative results were obtained in 20 of 21 bleeding points studied localizing the bleeding point within 3 to 6 cm.

5. Utilization of this experimental technique may be of great value in establishing the site of persistent and active intestinal bleeding of undetermined origin in the unusual patient in whom meticulous diagnostic studies have failed to disclose a bleeding lesion and exploratory laparotomy does not determine the origin of hemorrhage.

6. Doses of radioactivity varying from 10 to 20 microcuries have been utilized and are not considered hazardous to either the patient or the surgeon.

REFERENCES

1. Gray, H. K., Shands, W. C., and Thuringer, C.: The Problem of Massive Gastrointestinal Hemorrhage From an Undetermined Source, Ann. Surg. **139**: 731, 1954.
2. Harridge, W. H., Guynn, N. L., and Reynolds, J. T.: Diagnostic Procedures in Bleeding From the Gastrointestinal Tract, S. Clin. North America 83-92, Feb., 1956.
3. Oberhelman, H. A.: Diagnosis During Surgery, S. Clin. North America 169-176, Feb., 1956.
4. Patton, T. B., and Johnston, C. G.: A Method for the Control of Bleeding From Esophageal Varices, Arch. Surg. **59**: 502, 1949.
5. Sengstaken, R. W., and Blakemore, A. H.: Balloon Tamponade With Control of Hemorrhage From Esophageal Varices, Ann. Surg. **131**: 781, 1950.
6. Zamcheck, N., Chalmers, T. C., Ritvo, M., and Osborne, M. P.: Early Diagnosis in Massive Gastrointestinal Hemorrhage, J. A. M. A. **148**: 504, 1952.

GASTRIC RESECTION WITH END-TO-END CHOLECYSTODUODENOSTOMY IN A CASE OF DUODENAL ULCER WITH OBSTRUCTION TO COMMON BILE DUCT

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A MAN 48 years of age had experienced symptoms of duodenal ulcer periodically for 21 years. Early in the course of the disease the attacks of pain had tended to be mild and had yielded readily to simple nonsurgical treatment. In recent years the pain during attacks had been more severe, had been referred to the back, had wakened the patient often at night, and had stubbornly resisted nonsurgical treatment. An episode of melena with fainting had occurred 2 years before the present admission. Surgical treatment had been advised one year before the present admission but had been postponed when the patient's reluctance was strengthened by the improvement that followed redoubled efforts at nonsurgical management. But symptoms had recurred, vomiting had made its appearance, 20 pounds of body weight had been lost, and finally hematemesis and melena had come to dominate the picture. Subtotal gastrectomy was performed with removal of about 70 per cent of the stomach. Gastrointestinal continuity was re-established by a posterior Hofmeister-Polya type of gastrojejunostomy, but the duodenal ulcer and duodenal stump presented technical difficulties. The solution to these is the subject of this paper.

In the first and second portions of the duodenum was an ulcer 3 cm. in diameter which penetrated deeply into the head of the pancreas and the tissues over the distal part of the common bile duct. Because there had been bleeding from the ulcer only 24 hours earlier, I felt obliged to dissect it out. After the duodenum had been divided and dissected away from the pancreas until a free edge of intestine presented distal to the ulcer, I compressed the gall bladder, hoping to identify the ampulla of Vater by expressing bile through it. I was surprised to see a jet of bile spurt from a hole in the base of the ulcer (Fig. 1). Some bile also passed through the ampulla of Vater, which was about 2 cm. farther down the duodenum. Apparently the ulcer had perforated into the common bile duct. The patient had not been jaundiced before the operation. The common duct appeared normal in size and was explored; that part near the ulcer was very narrow and accepted a probe 4 mm. in diameter with great difficulty. Neither probe nor catheter could be passed through the bile duct into the duodenum. A T tube (No. 10 Fr.) was sutured into the common bile duct. Instead of closing the duodenal stump I anastomosed

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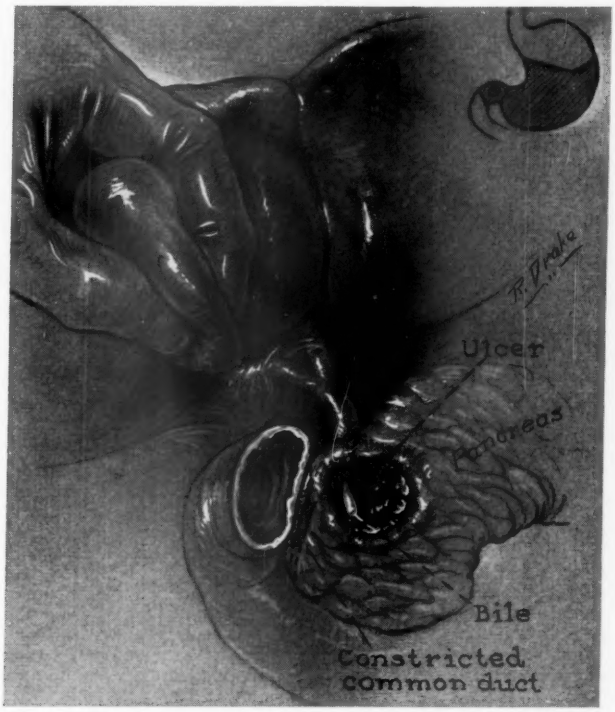

Fig. 1.—When the gall bladder was compressed a jet of bile spurted from a choledochoduodenal fistula in the base of the ulcer.

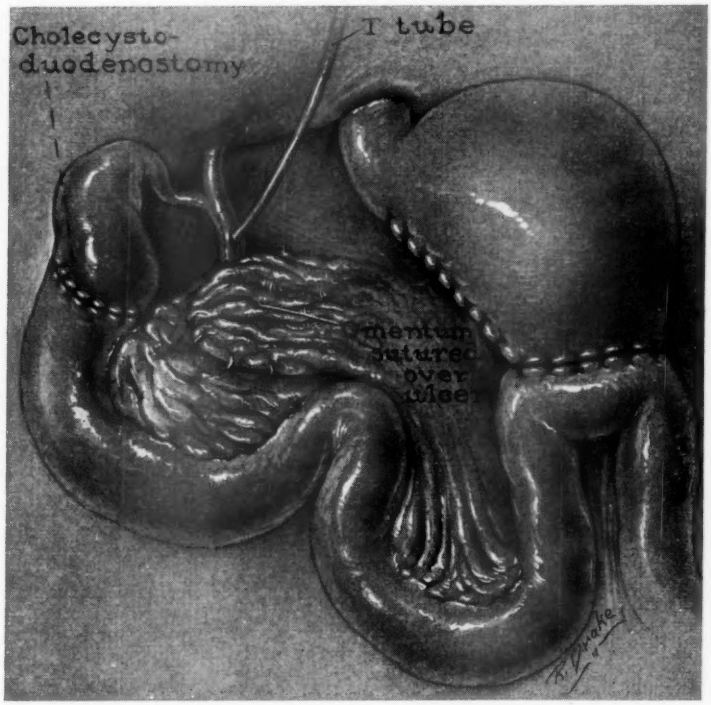

Fig. 2.—The fundus of the gall bladder anastomosed to the duodenal stump, with omentum sutured over the ulcer bed and a T tube placed in the common bile duct for temporary drainage.

it to the fundus of the gall bladder to prevent development of obstructive jaundice in the event that the inflammation narrowing the common bile duct did not subside (Fig. 2). No sutures were placed in the bed of the ulcer to close the fistula into the common duct, because it seemed that suturing might narrow the duct further. The ulcer crater was covered with omentum tacked to its edges as a pedicle graft. A Chaffin sump drain was placed to the region of the ulcer to remove any fistulous drainage which might occur.

From the seventh to the fifteenth day after operation pancreatic juice drained from the drain site, at first in quantities of 800 to 1,000 ml. per day and then in lesser amounts until drainage ceased. At no time did bile drain from the wound. It was demonstrated that the T tube could be clamped without the patient's becoming distressed. Serum bilirubin on the seventh day after operation was 1.2 mg. per cent direct and 0.9 indirect; on the twelfth day, 0.9 direct and 0.3 indirect. Stools were of normal color. Cholangiograms made by injecting radiopaque medium into the T tube showed that the lower end of the common duct was obstructed and that medium reached the duodenum via the gall bladder (Fig. 3). No drainage of bile followed removal of the T tube 26 days after operation.

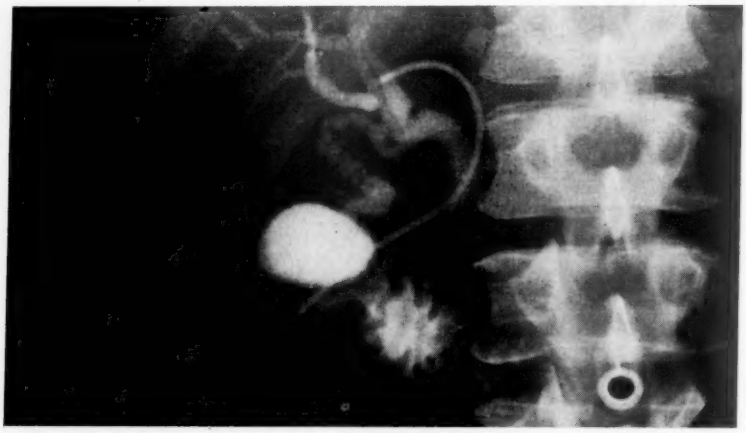

Fig. 3.—Postoperative T-tube cholangiogram. Radiopaque medium reaches duodenum via the gall bladder. The common bile duct appears completely obstructed.

When re-examined 10 months later the patient was found to weigh only 10 pounds less than his normal weight, to eat comfortably, and to be fully employed at heavy labor. He had noted no jaundice; the serum bilirubin measured directly was zero and that measured indirectly was 0.74 mg. per hundred milliliters. An intravenous cholangiogram showed the cholecystoduodenal anastomosis through which most of the medium appeared to enter the duodenum. Enough medium entered the lower end of the common bile duct to indicate that it was patent though narrowed. Some medium appeared to enter the duodenum through this route.

COMMENT

The best way to protect the common bile duct in surgical treatment of duodenal ulcer is to avoid dissection of ulcers which are so large or are placed

so distally that they encroach upon the region of the choledochus. If the usual type of gastric resection is to be done, all antral mucosa must be removed or the incidence of recurrent ulceration is great. For some ulcers 2 cm. or more beyond the pylorus, the duodenum can be divided and closed proximal to the ulcer, thus excluding it. If induration and ulceration preclude this, the surgeon can divide the pyloric antrum, excise the antral mucosa, and close the seromuscular portion of the antral stump—the so-called Bancroft procedure. Often the best procedure in the case of large duodenal ulcer associated with massive inflammatory reaction around the head of the pancreas and common bile duct is to avoid gastric resection and perform bilateral vagotomy and gastroenterostomy. It could be argued that this procedure might have been preferable in the case under discussion. However, when massive bleeding has occurred very recently, it is possible that bleeding may continue if the ulcer is left untouched. Also, when I began the dissection of this particular ulcer, I did not realize that it encroached upon the common duct. Soon after such a dissection is begun, a point of no return is reached. If dissection leads too close to the common bile duct, the surgeon can open the duct profitably and insert a catheter through it into the duodenum, as was suggested by Lahey and Marshall.[1] With the catheter in place, the course of the duct can be identified and the duct can be avoided.

In the case under discussion, however, the distal part of the common bile duct was so narrowed that probes and catheters could not be passed. Furthermore, there was a fistula between the duct and the base of the ulcer. Once these facts were known, it appeared likely that unless some provision was made for free drainage of bile into the intestine, a biliary fistula and, perhaps later, obstructive jaundice might occur. Anastomosis between gall bladder and duodenal stump seemed a ready solution to the problems of obstruction of the common bile duct and handling of the duodenal stump. Presumably the fate of this anastomosis will depend upon the status of the common bile duct. If the common duct becomes patent again as edema around the pancreas subsides, the opening formed by cholecystoduodenostomy could become stenosed and finally functionless.

I am sure others must have occasionally resorted to this device, although I have not encountered a description of it thus far.

This report, of course, is not presented to suggest a method to be used commonly in closing the duodenal stump. It is presented to suggest a way of handling the unusual problem of obstruction of the common duct by duodenal ulcer or of fistula between duct and ulcer.

REFERENCE

1. Lahey, F. H., and Marshall, S. F.: Surgical Management of Some of the More Complicated Problems of Peptic Ulcer, Surg., Gynec. & Obst. **76**: 641-648, 1943.

FECAL ENEMA AS AN ADJUNCT IN THE TREATMENT OF PSEUDOMEMBRANOUS ENTEROCOLITIS

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THE apparent increased incidence of pseudomembranous enterocolitis has renewed interest in the pathogenesis and clinical management of this disease.[2, 6, 10, 14] Even with the aid of modern supportive measures, a mean mortality of 74 per cent is found in 3 recently published series.[4, 8, 12] The purpose of this paper is to report the successful use of fecal enemas in the management of 4 such cases in the hope that more complete evaluation of this simple therapeutic measure can be given further clinical trial by others.

Finney[3] in 1893 reported a case of necrotizing enterocolitis following gastroenterostomy for pyloric ulcer and since that time many reviews of this subject have been published. There appear to be 2 general types of the disease: the one precipitated by intestinal obstruction, shock, or impairment of intestinal vascular supply[9] and the other caused purely by an overwhelming *Micrococcus pyogenes* (staphylococcus) enteritis. A number of these cases bear no relationship to surgical procedures. Although pure cultures of *Micrococcus pyogenes* (staphylococcus) are found in the stools in many of these cases, this is not an invariable finding.[12] Faulty bacteriologic isolation techniques have been suggested to account for this discrepancy.[8, 13] Most of the recently reported cases have followed the use of oral broad-spectrum antibiotics,[4, 8, 12, 13, 15] suggesting that the intestinal flora was thus altered to permit an overgrowth of antibiotic-resistant *Micrococcus pyogenes* (staphylococcus) within the gut. The relationship of these drugs to the disease is debatable inasmuch as the incidence of the disease may not have increased since their use.[11]

Because the mortality rate from pseudomembranous enterocolitis remains distressingly high despite the use of modern supportive measures and antibiotics effective against *Micrococcus pyogenes,* an attempt was made to re-establish the normal intestinal bacterial flora by the administration of normal feces into the colon of patients with the disease. This therapy is based upon the fact that staphylococcal overgrowth occurs when other organisms disappear and that reintroduction of the bacteria, viruses, and bacteriophage normally found in the colon might re-establish the balance of nature with subsidance of staphylococcal predominance and the distressing symptoms caused thereby.

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CASE REPORTS

CASE 1.—A. R., a 46-year-old Spanish-American, underwent a Billroth II gastric resection on April 28, 1957, because of massive bleeding from a diffuse hemorrhagic gastritis. Postoperatively he had elevated temperature and received a mixed antibiotic regime as illustrated in Fig. 1. On the fifth postoperative day he developed abdominal distention, vomiting, bloody diarrhea, and marked hypotension and was given vasopressors and hydrocortisone. On the seventeenth postoperative day a laparotomy was performed because of a question of small bowel obstruction, but none was found. Two days following this operation he again developed copious bloody diarrhea and the diagnosis of pseudomembranous enterocolitis was first entertained. Immediate stool culture revealed *Micrococcus pyogenes* (hemolytic, coagulase positive *Staphylococcus aureus*). Despite adequate fluid therapy, cortisone, and Albamycin, his diarrhea continued unabated and he appeared to be in the terminal stages of his critical illness. On May 23, 1957, after another stool culture grew out pure *Micrococcus pyogenes,* a retention fecal enema was administered using donor feces from a normal subject who had received no antibiotics during the previous several months. On the following day there was marked improvement in his general condition and his bloody diarrhea ceased. Stool culture on the following day, May 24, revealed no *Micrococcus pyogenes,* and another fecal enema was administered on that day. The patient improved very rapidly and was discharged from the hospital 10 days later, completely asymptomatic.

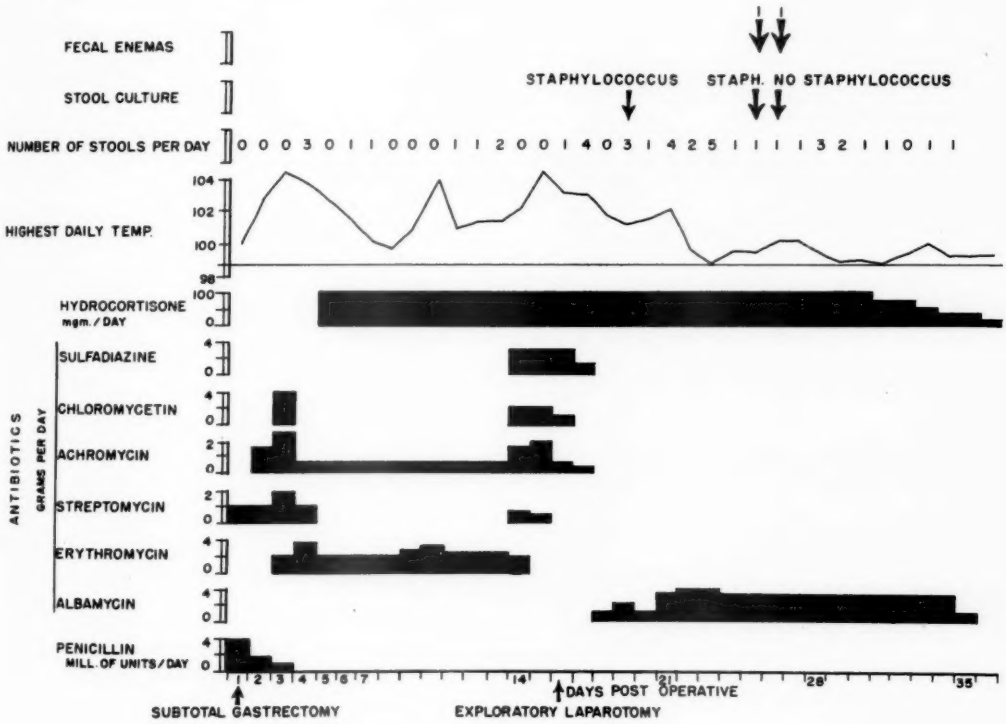

Fig. 1.—Case 1.

Comment: There was an immediate and dramatic response by this critically ill patient to a fecal retention enema. The bloody diarrhea stools which grew pure cultures of *Micrococcus pyogenes* stopped within a few hours and staphylococci disappeared from the stools.

CASE 2.—O. H., a 65-year-old white man, underwent subtotal gastrectomy with a tube duodenostomy on Dec. 24, 1957, for an acute perforating, bleeding, and obstructing duodenal ulcer. His course was uneventful until the fifth postoperative day, when he developed signs of peritonitis. Exploratory laparotomy revealed no leakage around the duodenostomy tube.

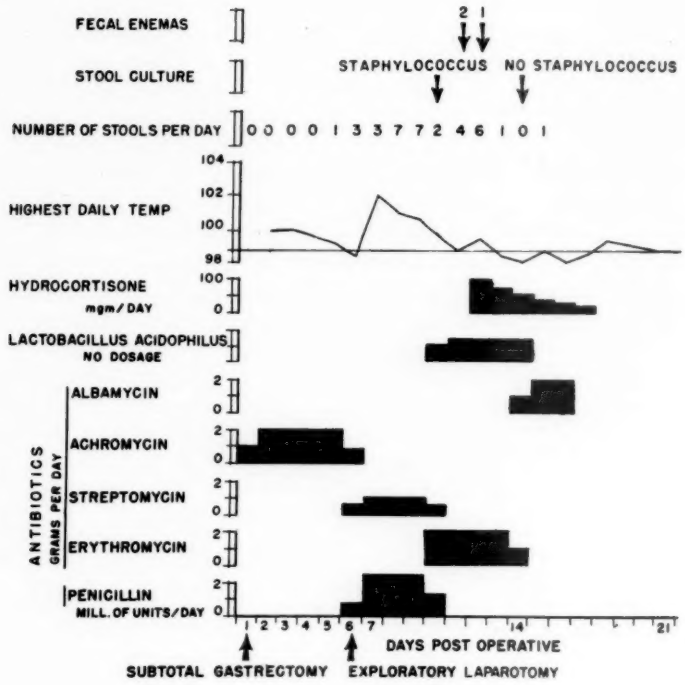

Fig. 2.—Case 2.

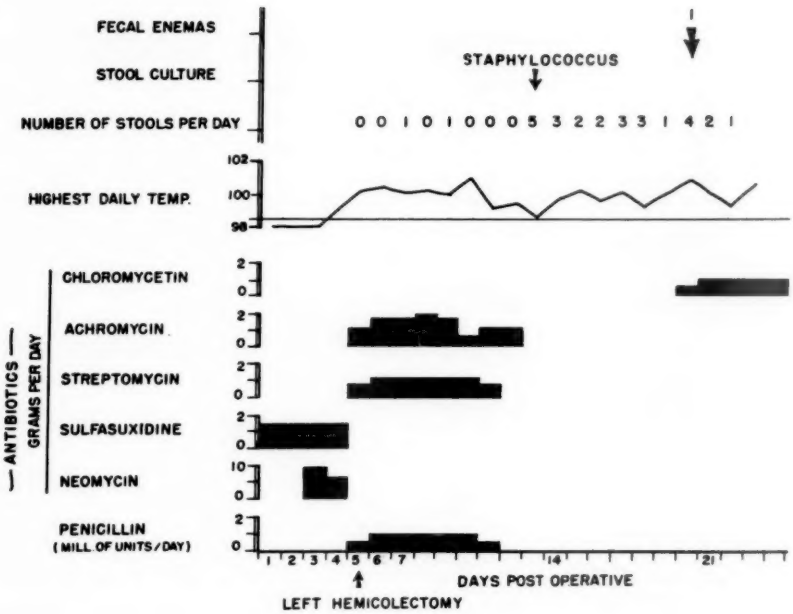

Fig. 3.—Case 3.

Twenty-four hours later the patient began having frequent loose, mucoid, greenish bowel movements. On the fourth postoperative day as his diarrhea stools increased, he suddenly went into profound shock which required heroic fluid and electrolyte replacement. Smears and cultures of stool at this time revealed *Micrococcus pyogenes* (hemolytic, coagulase positive *Staphyloccus aureus*). Hydrocortisone and erythromycin were added to his therapy with but little improvement. On Jan. 3, 1958, 2 fecal retention enemas were given and another the following day. Diarrhea stopped within 48 hours and *Micrococcus pyogenes* had entirely disappeared from the stool 4 days after the administration of the first fecal enema. Fig. 2 illustrates the complex antibiotic regimen maintained on this patient and his response following the fecal enemas.

Comment: This patient became desperately ill with pseudomembranous enterocolitis 9 days following operation. His progressive and totally resistant staphylococcal diarrhea resulted in profound shock and he appeared moribund. Clinical response to fecal enemas was dramatic with disappearance of the diarrhea and a return of normal bacterial flora in the stools.

Case 3.—C. P. (Fig. 3), a 68-year-old white man, underwent left hemicolectomy with end-to-end anastomosis for a carcinoma of the descending colon on Jan. 22, 1958. Sulfasuxidine and neomycin were used preoperatively for preparation of the colon. Achromycin, penicillin, and streptomycin were administered postoperatively. His immediate course was uneventful, but 8 days following surgery he developed profuse watery diarrhea and a low-grade fever, which persisted for one week. Cultures of the stool revealed *Micrococcus pyogenes* (hemolytic, coagulase positive *Staphylococcus aureus*) in pure culture. A fecal retention enema was given and within 48 hours the diarrhea had completely ceased. The patient was discharged 5 days later.

Comment: This man represents a milder variety of staphylococcal enterocolitis. The cessation of symptoms following institution of therapy was abrupt.

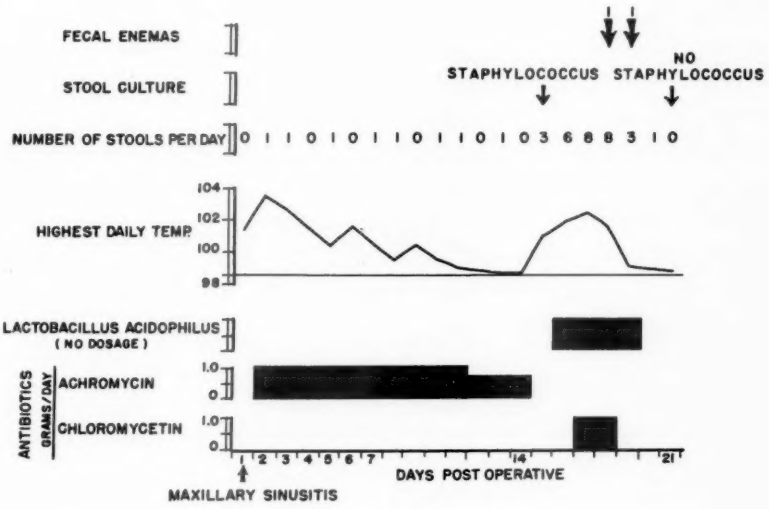

Fig. 4.—Case 4.

Case 4.—N. D. (Fig. 4), a 45-year-old woman, received Achromycin, 1 Gm. daily, for acute beta-hemolytic streptococcal maxillary sinusitis. After 2 weeks of therapy the fever and toxicity abated, but 3 days thereafter, while still receiving antibiotics, she suddenly developed profuse watery and bloody diarrhea and recurrence of fever. Stool cultures grew pure *Micrococcus pyogenes* (hemolytic, coagulase positive *Staphylococcus aureus*) sensitive to Chloromycetin. Intramuscular Chloromycetin was administered but neither this drug nor acidophilus milk affected the fever, toxicity, or severe bloody diarrhea. Intravenous fluid and electrolyte replacement was required in heroic proportions.

Four days after the onset of the bloody diarrhea when all other therapeutic methods had failed, a fecal retention enema was administered to the patient and repeated the next day. Within 24 hours of the first enema the diarrhea had ceased and stool cultures revealed no further hemolytic staphylococci. The patient made an uneventful recovery.

Comment: This patient developed pseudomembranous enterocolitis following a 2-week course of broad-spectrum antibiotics. Severe and life-threatening staphylococcal diarrhea was resistant to all other forms of therapy but responded dramatically to fecal enemas.

DISCUSSION

Three of these 4 patients with pseudomembranous enterocolitis almost succumbed to disease before fecal enemas were employed. In all 4 patients, hemolytic coagulase positive *Staphylococcus aureus* was found in large numbers in the stool, both by smear and by culture prior to the fecal retention enemas, and staphylococci disappeared following this therapy. In order to evaluate scientifically the efficacy of fecal enemas in the therapy of pseudomembranous enterocolitis, it would be necessary to withhold other forms of treatment, an unjustifiably stringent experiment in view of the gravity of the illness.

In many cases staphylococci seem to play a key role in the pathogenesis of pseudomembranous enterocolitis and their disappearance from the stool is accompanied by clinical improvement. Chemotherapeutic measures remain relatively ineffective in this as well as other types of staphylococcal infections, so that other measures must be attempted.

Van Prohaska[13] has suggested that staphylococci cannot flourish in the intestinal tract in the presence of the normal colonic flora. Taking advantage of this fact it seems reasonable to attempt to re-establish the varied bacterial habitants of the bowel when they have temporarily been replaced by a pathogenic strain of staphylococcus. Substitution of enteric nonpathogens as a therapeutic measure has been given previous trial, by feeding of acidophilus milk.[14]

Unfortunately, there is no method for producing pseudomembranous enterocolitis in the experimental animal and thus to evaluate therapeutic measures under controlled conditions. The apparent association of the use of broad-spectrum oral antibiotics with the disease suggests the trial of these drugs in precipitating such an enteritis. Van Prohaska[13] has been unable thus to produce the disease in monkeys and kittens, and we have had similar unsuccessful results in dogs. Dack[1] fed large doses of *Micrococcus pyogenes* to human volunteers and was seldom able to recover the organisms in the stools.

In the hope of precipitating staphylococcal enteritis within a previously sterilized segment of bowel we constructed a Thiery fistula consisting of the large bowel from the ileocecal valve to the sigmoid flexure in 2 adult dogs. After mechanical cleansing, these isolated segments were lavaged twice daily with Achromycin solutions for 4 days until sterility was approached. Large doses of a pure broth culture of Achromycin-resistant *Micrococcus pyogenes* (coagulase positive hemolytic *Staphylococcus aureus*) then were instilled into the proximal stoma of the isolated intestinal segment daily for 4 days. Even this technique did not produce a progressive enteritis or bloody diarrhea from the isolated colonic segment.

Should further clinical experience substantiate the beneficial effect of fecal enemas in the treatment of pseudomembranous enterocolitis,[5] more precise bacterial, viral, or bacteriophage substitution therapy might be employed. Since the disease occasionally involves parts of the intestinal tract proximal to the colon, the oral administration of pure cultures of these organisms in enteric-coated capsules might be both more aesthetic and more effective.

SUMMARY

1. Retention enemas composed of normal feces suspended in saline have been administered to 4 patients with pseudomembranous enterocolitis. In each instance the clinical course was markedly improved and the *Micrococcus pyogenes* (staphylococcus) which grew in pure culture prior to treatment disappeared from the stools and was replaced with normal colonic nonpathogens following such therapy.

2. Unsuccessful efforts to produce the disease in experimental animals are described.

3. It is suggested that this simple yet rational therapeutic method should be given more extensive clinical evaluation.

REFERENCES

1. Dack, G. M.: Food Poisoning, Ed. 2, Chicago, 1949, University of Chicago Press.
2. Findland, M., and Weinstein, L: Complications Induced by Antimicrobial Agents, New England J. Med. **248**: 220-226, 1953.
3. Finney, J. M. T.: Gastroenterostomy for Cicatrizing Ulcer of the Pylorus, Bull. Johns Hopkins Hosp. **4**: 53-54, 1893.
4. Frank, L., and Avola, F. A.: Pseudomembranous Enterocolitis as a Postoperative Complication, Gastroenterology **29**: 391-402, 1955.
5. Kersten, H. M.: Intentional Replacement of Bacteria Following Antibiotic Therapy, J. Iowa Med. Soc. **48**: 240, 1958.
6. Kleckner, M. S., Jr., Bargen, J. A., and Baggenstoss, A. H.: Pseudomembranous Enterocolitis: Clinicopathologic Study of Fourteen Cases in Which the Disease Was Not Preceded by an Operation, Gastroenterology **21**: 212-222, 1952.
7. Markley, J. C., Carson, R. J., and Holzer, C. E.: Pseudomembranous Enterocolitis: A Clinicopathologic Study of Thirteen Cases With a Common Etiologic Factor, A. M. A. Arch. Surg. **77**: 1958.
8. Newman, C. R.: Pseudomembranous Enterocolitis and Antibiotics, Ann. Int. Med. **45**: 409-444, 1956.
9. Penner, A., and Bernheim, A. I.: Acute Postoperative Enterocolitis: A Study on the Pathologic Nature of Shock, Arch. Path. **27**: 966-983, 1939.
10. Penner, A., and Druckerman, L. J.: Enterocolitis as a Post-Operative Complication and Its Significance, Gastroenterology **11**: 478-487, 1948.
11. Pettet, J. D., Baggenstoss, A. H., Dearing, W. H., and Judd, E. S., Jr.: Postoperative Pseudomembranous Enterocolitis, Surg., Gynec. & Obst. **98**: 546-552, 1954.
12. Prohaska, J. V., Govostis, M. C., and Taubenhaus, M.: Postoperative Pseudomembranous Enterocolitis: Successful Treatment With Corticotropin (ACTH), J. A. M. A. **154**: 320-323, 1954.
13. Prohaska, J. V., Long, E. T., and Nelsen, T. S.: Pseudomembranous Enterocolitis: Its Etiology and the Mechanism of the Disease Process, A. M. A. Arch. Surg. **72**: 977-983, 1956.
14. Reiner, L., Schlesinger, M. J., and Miller, G. M.: Pseudomembranous Colitis Following Aureomycin and Chloramphenicol, A. M. A. Arch. Path. **54**: 39-67, 1952.
15. Rettger, L. F., and Cheplin, H. A.: Lactobacillus Acidophilus and Its Therapeutic Application, Arch. Int. Med. **29**: 357, 1922.
16. Terplan, K., Paine, J. R., Sheffer, J., Egan, R., and Lansky, H.: Gastroenterocolitis Caused by Staphylococci: Its Apparent Connection With Antibiotic Medication, Gastroenterology **24**: 476-509, 1953.

THE RISK OF SECTION OF THE SPHINCTER OF ODDI
An Animal Experiment

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INTRODUCTION

THE division of the sphincter of Oddi, sphincterotomy or sphincteroplasty, has been used in the surgical management of pancreatitis,[4, 9, 19] choledocholithiasis, the finding of a stenosed or fibrotic sphincter during choledochal exploration,[3] postcholecystectomy syndrome, and pancreatic pseudocysts.[5] Variable follow-up results have been published. Postoperative complications, such as stricture and ascending cholangitis,[15] and fatalities due to acute pancreatitis[1, 16] have been reported. An evaluation of the results of sphincterotomy will not be made in this study. The investigation was designed to determine the cause of the complications and the magnitude of the risk involved.

METHOD

Fifteen adult cats were anesthetized with intraperitoneal barbiturate solution. Through an upper abdominal midline incision, biopsies of the liver and tail of the pancreas were taken. The gall bladder was removed to simulate the conditions which would exist in the human being following sphincterotomy. A duodenotomy was placed opposite the papilla of Vater. The orifice in the duodenal papilla was probed and dilated. The directions of the choledochus and main pancreatic duct were determined. Cats were chosen because the anatomic relationships of the extrahepatic and pancreatic ductal systems closely resemble those of the human being.[7] In each of the animals the pancreatic duct was found to join the common bile duct near the duodenum and terminate in a common channel. Using fine scissors, an elliptical wedge of the sphincter of Oddi, about 2 by 2 by 6 mm., approximately one-sixth of the circumference, was excised. No sutures were used in the wound of the papilla. The duodenal and abdominal incisions were closed. Intramuscular penicillin and streptomycin were given on the day of surgery and for 4 postoperative days. Cat food and water were offered. At various intervals autopsy examinations were performed.

At autopsy, sections of liver and pancreas were taken. The block of pancreas was cut near the termination of the common bile duct and the main

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pancreatic duct where maximal effect and inflammation from duodenal reflux might be expected. The appearance of the sphincterotomy site was noted.

In 4 control animals, the procedure was identical except the sphincter of Oddi was not disturbed.

All specimens of tissues removed were studied microscopically by the staff pathologist, Dr. Nancy Warner.

RESULTS

There were no pathologic findings in the sections of the biopsies taken at the time of the sphincterotomy.

Cats do not thrive well when caged in the laboratory. Five of the animals (Cats 1, 2, 6, 14, and control 2) expired after varying lengths of time (4 to 110 days). The autopsy examinations were carried out as in the others.

Several of the cats ate poorly and the resulting malnutrition might have accounted for the fatty infiltration present in the liver sections of 7 (Cats 2, 5, 6, 7, 8, 9, and 10). No other lesions were seen in the specimens of liver. There was no ascending cholangitis observed.

Inspections of the sphincterotomy site revealed smooth healing in every instance except one (Cat 10). This animal survived 3 months. At the site of the wedge excision in the papilla, a pile-up of granulation tissue was found. The orifice was patent. There was no evidence of stricture formation, ductal dilatation, or biliary stasis in any of the animals.

The pancreas revealed no gross changes. In those examined during the first postoperative week, the microscopic study revealed acute inflammatory reactions. In Cat 1, an acute pancreatitis was present (Fig. 1). In the others

TABLE I

NUMBER	SURVIVED DAYS	MICROSCOPIC FINDINGS IN PANCREATIC TISSUE REMOVED AT AUTOPSY EXAMINATION
1	4	Neutrophilic infiltration of interstitial areas and pancreatic lobules, fibrinopurulent exudate within wall, and lumen of pancreatic duct with necrosis, foci of fat necrosis
2	4	Interstitial neutrophilic infiltration
3	7	Interstitial neutrophilic infiltration, fibrinopurulent exudate of peripancreatic tissues, foci of fat necrosis
4	7	Organizing and subsiding inflammation of peripancreatic tissues, leukocytic interstitial infiltration
5	49	Isolated foci of lymphocytic infiltration
6	70	Normal
7	84	Normal
8	84	Normal
9	84	Slight lymphocytic infiltration wall of large pancreatic duct
10	84	Normal
11	84	Normal
12	84	Normal
13	112	Normal
14	110	Minimal lymphocytic infiltration wall of large pancreatic duct
15	168	Normal
Controls		
1	28	Normal
2	4	Neutrophilic infiltration of interstitial areas and walls of few small ducts with exudate in lumina
3	7	Normal
4	7	Normal

Fig. 1.

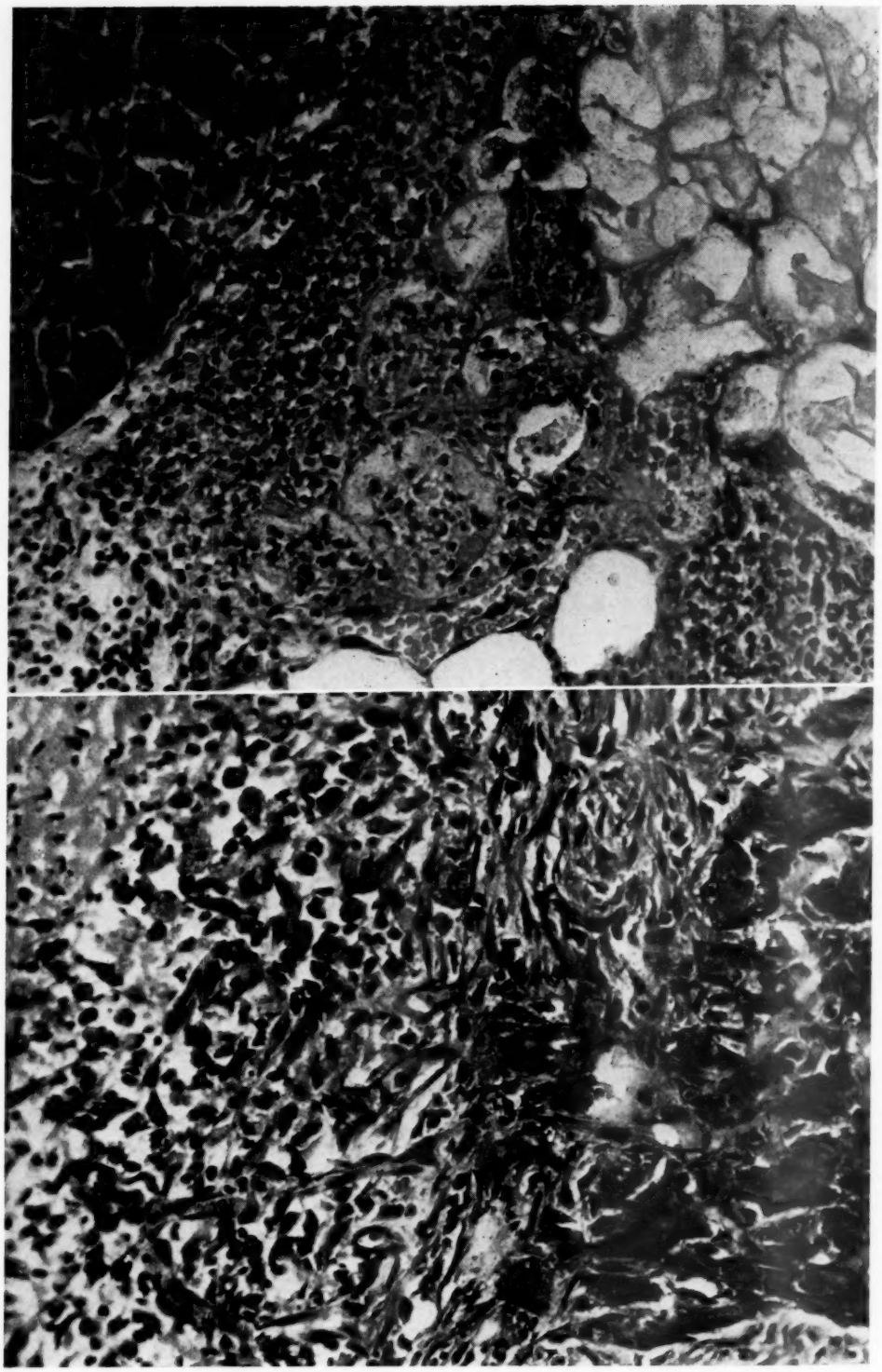

Fig. 2.

Fig. 1.—Neutrophilic infiltration and fat necrosis of the pancreas in Cat 1, survived 4 days following sphincterotomy.

Fig. 2.—Interstitial neutrophilic infiltration of the pancreas in Cat 3, survived 7 days after sphincterotomy.

Fig. 3.

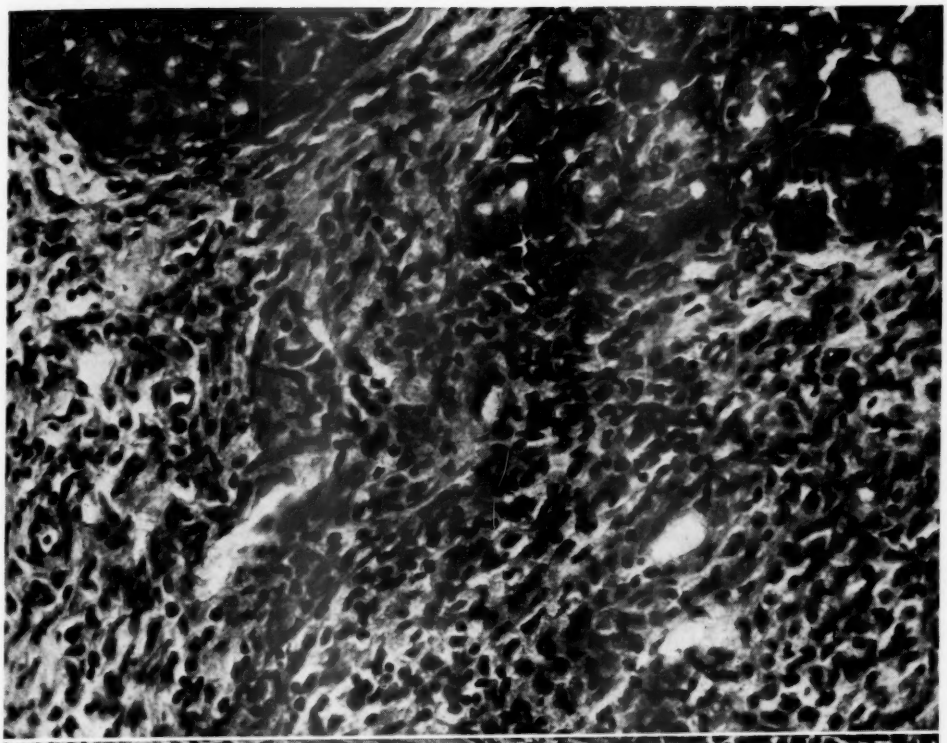

Fig. 4.

Fig. 3.—Organizing inflammation of peripancreatic tissues and leukocytic interstitial infiltration in Cat 4, survived 7 days after sphincterotomy.

Fig. 4.—Interstitial neutrophilic infiltration of pancreas in control Cat 2, survived 4 days after sphincterotomy.

of the early group (Cats 2, 3, and 4), the reaction was located mostly in the interstitial spaces (Figs. 2 and 3). In those examined after survival of 7 to 24 weeks, there were practically no microscopic abnormal findings.

In one of the control group (Cat 2) an acute inflammatory reaction, especially in the interstitial areas, was present (Fig. 4). The microscopic examination of the pancreas in the other three (Cats 1, 3, and 4) failed to reveal any reaction.

The result of the study of the pancreatic tissue is summarized in Table I.

DISCUSSION

There were no findings to support the thought that sphincterotomy renders the sphincter mechanism of the common bile duct and main pancreatic duct incompetent. Boyden[2] pointed out that the papillary sphincter is but a part of a complicated sphincter mechanism which includes the duodenal musculature and separate pancreatic duct and choledochal sphincters (Fig. 5). To destroy the sphincter mechanism completely it would be necessary to interrupt the sphincteric muscles within the duodenal wall and even go a little beyond the limits of the duodenal wall. Under normal conditions the secretory pressures of the liver and pancreas have been found to be greater than the duodenal intraluminal pressures.[11] Occasionally duodenal pressures increase and are greater than the falling secretory pressures of the liver and pancreas,[12] a phenomenon which occurs following a major abdominal surgical procedure. There were no signs of duodenal regurgitation in these experiments (Fig. 6), further supporting the competency of the sphincteric mechanism. No cholangitis was observed. In only one (Cat 1) was there found inflammation in the pancreatic duct, fibrinopurulent exudate in the lumen, and necrosis of the wall. During the instrumentation, infected duodenal juices gain entry into the pancreatic duct and, perhaps by activation of trypsinogen at that site, cause inflammation.

The acute interstitial inflammatory reactions observed during the first postoperative week were due to trauma. During the manipulation, pancreatic acini are compressed with the leakage of enzymes into the interstitial spaces. The inflammation seen in these sections is the result. There were no chronic changes in the pancreas following sphincterotomy such as reported by Mallet-Guy[10] in his series of animal experiments.

Experimentally, the transition from an edematous and interstitial pancreatitis to a necrotic type has been demonstrated.[13] Occasionally, this phenomenon occurs in the human being following blunt and operative trauma. Investigators[6, 8] have explained such occurrences on the basis of trauma and in combination with other factors, obstruction of the pancreatic duct in various ways, interference with the blood supply to the pancreas, and infection. Powers and associates[14] suggested, following their experiments, that with pancreatic duct obstruction the secreted trypsinogen increases to a high concentration within the pancreas. Hemorrhagic and necrotic pancreatitis occurs when the

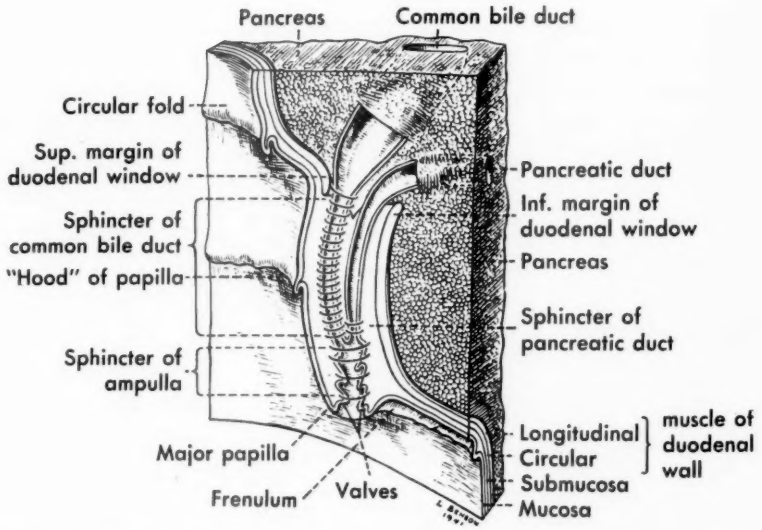

Fig. 5.—Diagram of the sphincter of Oddi (From Hollingshead, W. H.: Anatomy for Surgeons, New York, 1956, Paul B. Hoeber, Inc., Vol. 2; relabeled from Boyden, E. A.: SURGERY 10: 567, 1941).

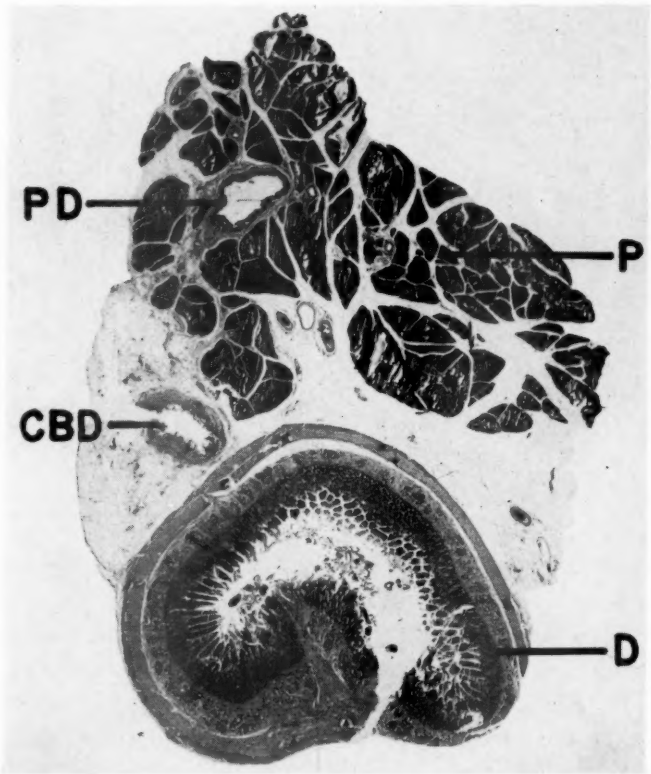

Fig. 6.—Specimen of pancreas (*P*) and duodenum (*D*) near the termination of the common bile duct (*CBD*) and main pancreatic ducts (*PD*), Cat 8, 3 months following sphincterotomy.

inactive enzyme is activated. The activator may be bile, enterokinase, infection, or trypsin in the circulating blood, which occurs following trauma, extensive surgery, or tissue destruction.

Thompson and co-workers[18] recently collected 75 reported cases of acute pancreatitis following biliary tract surgery, particularly choledochotomy. This postoperative complication following choledochal exploration is explainable.

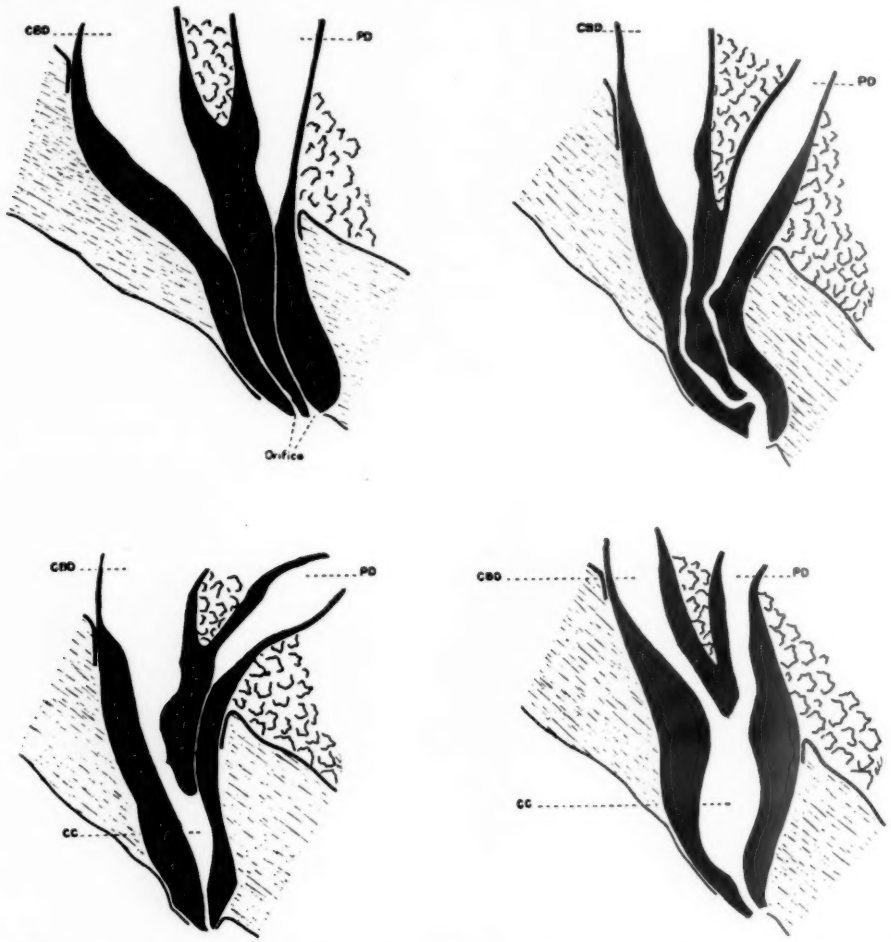

Fig. 7.—Drawings of specimens of the papilla of Vater[18] (From Sterling, J. A.: Surg., Gynec. & Obst. 98: 420-424, 1954).

The anatomic arrangement of the terminations of the pancreatic and common bile ducts has been studied.[17] Measurements of these ducts at their distal ends reveal them to be minute, approximately 1 mm. in diameter. A septum containing a projection of pancreatic tissue has been seen in the specimens studied (Fig. 7). Mechanical trauma with the probe, dilator, scoop, or scalpel, with the resultant edema and inflammatory reaction of the septum and surrounding pancreatic tissue, causes narrowing and obstruction of the termination of the pancreatic duct and possibly acute pancreatitis. The introduction of infected duodenal juices into the pancreatic ductal system might also be a contributing factor.

SUMMARY

Sphincterotomy was performed in 15 cats. No complications attributable to the procedure were encountered except those due to trauma in the region of the sphincter of Oddi and head of the pancreas. Acute inflammation in the pancreas was demonstrated. The cause of this reaction and the mechanism of the transition of edematous or interstitial pancreatitis to necrotic pancreatitis were discussed.

The risk of inducing acute pancreatitis in varying degrees while performing a sphincterotomy is recognized.

REFERENCES

1. Blatherwick, N. H., and Pattison, A. C.: Acute Pancreatitis Complicating Choledochal Sphincterotomy, Am. J. Surg. **88**: 129-135, 1954.
2. Boyden, E. A.: The Anatomy of the Choledochoduodenal Junction in Man, Surg., Gynec. & Obst. **104**: 641-652, 1957.
3. Cattell, R. B., Colcock, B. P., and Pollack, J. L.: Stenosis of the Sphincter of Oddi, New England J. Med. **256**: 429-435, 1957.
4. Doubilet, H., and Mulholland, J. H.: Eight-Year Study of Pancreatitis and Sphincterotomy, J. A. M. A. **160**: 521-528, 1956.
5. Doubilet, H., Poppel, M. H., and Mulholland, J. H.: Pancreatography—Indications and Observations, J. A. M. A. **163**: 1027-1030, 1957.
6. Dunphy, J. E., Brooks, J. R., and Ackroyd, F.: Acute Postoperative Pancreatitis, New England J. Med. **248**: 445-451, 1953.
7. Field, H. E., and Taylor, M. E.: An Atlas of Cat Anatomy, Chicago, 1950, University of Chicago Press.
8. Frieden, J. H.: Postoperative Acute Pancreatitis, Surg., Gynec. & Obst. **102**: 139-144, 1956.
9. Jones, S. A., and Smith, L. L.: Transduodenal Sphincteroplasty for Recurrent Pancreatitis, Ann. Surg. **136**: 937-947, 1952.
10. Mallet-Guy, P., Feroldi, J., and Gangolphe, M.: Pancréatites chroniques expérimentales, Lyon Chir. **51**: 323-331, 1956.
11. Parry, E. W., Hallenback, G. A., and Grindlay, J. H.: Pressures in the Pancreatic and Common Ducts, A. M. A. Arch. Surg. **70**: 757-765, 1955.
12. Popper, H. L., and Necheles, H.: Pancreatic Injuries: An Experimental Study, Surg., Gynec. & Obst. **93**: 621-624, 1951.
13. Popper, H. L., Necheles, H., and Russell, K. C.: Transition of Pancreatic Edema Into Pancreatic Necrosis, Surg., Gynec. & Obst. **87**: 79-82, 1948.
14. Powers, S. R., Brown, H. H., and Stein, A.: The Pathogenesis of Acute and Chronic Pancreatitis, Ann. Surg. **142**: 690-697, 1955.
15. Reynolds, J. T., and Laxy, B. G.: The Indications, Hazards and Contraindications for Division of the Sphincter of Oddi, S. Clin. North America **35**: 129-149, 1955.
16. Smith, S. W., Barker, W. F., and Kaplan, L.: Acute Pancreatitis Following Transampullary Biliary Drainage, SURGERY **30**: 695-700, 1951.
17. Sterling, J. A.: The Common Channel for Bile and Pancreatic Ducts, Surg., Gynec. & Obst. **98**: 420-424, 1954.
18. Thompson, J. A., Howard, J. M., and Vowles, K. D.: Acute Pancreatitis Following Choledochotomy, Surg., Gynec. & Obst. **105**: 706-710, 1957.
19. Warren, K. W.: Surgical Considerations in the Management of Chronic Relapsing Pancreatitis, S. Clin. North America **35**: 785-799, 1955.

CHOLEDOCHOSTOMY

A Follow-Up Report

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A PERIODIC review of cases requiring surgical exploration of the common bile duct is of value in a hospital where such operations are performed frequently. Since this surgical procedure is relatively standardized, a careful study of the cases will show not only the immediate results of such treatment but also the long-term results that indicate which patients require reclassification in terms of their end results.

The actual technique of choledochostomy as performed in this hospital has remained essentially the same for many years. Operative cholangiography has been used in only a small number of cases. There have been certain modifications affecting the selection of patients, the most notable being the frequent use in recent years of preoperative intravenous cholangiography. This has been applied with greatest frequency to cases with persistent or recurrent symptoms after previous biliary tract operations. Patients can be placed according to preoperative symptoms and findings into groups with varying and estimable incidences of common bile-duct obstruction. It is important in selection of patients to be aware of the differences in probability of duct obstruction which are implied by certain findings.

Ideally, only those cases with correctable obstruction would be selected for surgical exploration. Although this report does not include data on the morbidity and mortality rates for cholecystectomy plus duct exploration, these rates were found to be greater than those recorded for cholecystectomy alone. The additive effect of common bile-duct exploration on complication rates was present even in cases with negative results, that is, cases in which exploration revealed no abnormalities affecting the common bile duct. Therefore, it cannot be said that negative choledochostomies are not without potential harm.

In 1948 a report was made by Buxton and Burk[2] concerning 439 cases involving common bile-duct exploration at this hospital between 1934 and 1946. There was noted a progressive decline in operative mortality and morbidity, which could be attributed to improved pre- and postoperative treatment. According to their report, calculi were recovered from the ducts in 43 per cent of the cases. There was a 5.9 per cent incidence of stones retained in the ducts after the initial operation.

The study reported here represents a 10-year extension of the earlier study and covers the 1946 to 1956 period at the same hospital. Our recent experience

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will be combined with that of other authors on this subject in order to show the ways in which a high percentage of good results can be maintained after choledochostomy.

MATERIAL

There were 350 consecutive cases in which choledochostomy was performed to rule out the presence of stones in the common bile duct. Patients with malignant disease involving the biliary tract were excluded, as were those with duct strictures clearly originating as a result of operative trauma. Cases in which the duct was opened for identification, as for example during gastrectomy, were not included. The surgical treatment of the biliary tract that some of these patients required prior to choledochostomy at this hospital is outlined in Table I.

TABLE I

Primary choledochostomy patients		334
No previous biliary operations	234	
Cholecystectomy elsewhere	67	
Cholecystostomy	26	
Cholecystectomy at University Hospital	7	
Patients presenting for a secondary choledochostomy		16
First choledochostomy elsewhere	11	
First choledochostomy at University Hospital prior to 1946	5	
Total	350	350

There were only 7 patients in the group who had previously undergone cholecystectomy at this hospital, showing that nearly all cases with indications for choledochostomy were appropriately treated at the same time the gall bladder was removed. The smallness of this figure further demonstrates a rather liberal interpretation of the indications for choledochostomy. Stones were recovered from the ducts in 2 of these 7 patients; however, the time interval between cholecystectomy and recovery of the duct stones was 4 years in one instance and less than 3 months in the other. This latter case represents a clear instance in which there was an erroneous omission of duct exploration at the time of cholecystectomy.

There were 44 repeat operations for common bile-duct exploration in which the first choledochostomy also had been done at the University Hospital. Five cases were carried forward from the earlier reported series from this hospital, while the other 39 cases followed a primary choledochostomy within the 1946 to 1956 period. Eleven patients had had common bile-duct explorations elsewhere before admission to the University Hospital, bringing the total of repeat explorations in this series to 55. This report concerns the results of 389 common bile-duct explorations performed on 350 patients.

INDICATIONS FOR COMMON BILE-DUCT EXPLORATION

The most important single symptom indicating the need for choledochostomy is obstructive jaundice. In this study, 50 per cent of the patients with histories of either recent or remote icterus were found at the time of operation

to have obstruction of the bile duct. This obstruction was most frequently caused by stones, less often by inflammatory strictures from stone lodgment or passage, and in rare instances from chronic pancreatitis. When the jaundice was accompanied by chills and fever, the incidence of duct obstruction was 70 per cent. McKittrick and Wilson[5] have reported a similar high incidence of common bile-duct obstruction in cases which showed cholangitis. One-eighth of the patients in this series from the University Hospital had symptoms of cholangitis, and as such they represented a group with an absolute indication for choledochostomy.

The preoperative intravenous cholangiogram using Cholografin* has assumed great diagnostic importance, especially in evaluating patients with suspected functional disorders and those who have had previous biliary operations. If common bile-duct dilatation is shown, the presence of obstruction is inferred. The films are often of such quality that an offending stone can be seen. The most serious limitation is the lack of excretion of Cholografin into the ducts in the presence of deep jaundice; however, the jaundice itself is often the necessary evidence for exploration.

Obstruction revealed by direct cholangiography in the operating room is another absolute indication for choledochostomy. A fine polyethylene catheter can be passed through the cystic duct stump or directly into the common bile duct and an x-ray film can be exposed while 35 per cent Urokon sodium† is being injected. If care is taken to avoid injecting bubbles of air and to have the anesthetist control breathing during exposure of the film, a satisfactory x-ray is usually obtained. The film is processed and interpreted by the radiologist while the surgeon is performing other steps in the operation. If a technically unsatisfactory film is obtained, the x-ray is repeated. Thomson[6] states that a negative choledochograph should be obtained at the time of cholecystectomy in all cases before a decision is made to omit common bile-duct exploration. In spite of technical imperfections and occasional errors of interpretation, films have the advantage of being substantive records for the surgeon's use at a later time.

In addition to those cases in which choledochostomy was absolutely indicated, a group of patients remained with only relative indications for common duct exploration. The incidence of stone recovery from the common bile ducts of these patients was somewhat lower than the 34 per cent average for the entire group. This group included gall bladder patients with: (1) an earlier diagnosis of hepatitis to explain jaundice, (2) stones small enough to pass through the cystic duct, and (3) chronologically remote episodes of jaundice. Consideration of choledochostomy is required for patients with a history of biliary colic when the gall bladder is absent or when it does not contain stones. These cases showing relative indications for duct exploration are the ones in which the preoperative intravenous cholangiogram and the direct cholangiogram in the

*Cholografin—Squibb's iodipamide.
†Urokon Sodium—Mallinckrodt' S sodium acetrizoate.

operating room are of great aid. A negative operative cholangiogram in a borderline case will prevent further manipulation of normal ducts, and the patient will be spared the temporary inconvenience of a T tube. Needless explorations of tiny, thin-walled ducts must be avoided. In such cases on rare occasions inflammatory strictures have occurred at the point of exit of the T tube through the wall of the bile duct. It is the practice at this hospital to close the common bile duct around a T tube or catheter after exploration and to drain the space of Morison after all biliary tract operations.

TABLE II. INDICATIONS FOR CHOLEDOCHOSTOMY

1. Obstructive jaundice
2. Recurrent cholangitis
3. Intravenous cholangiogram showing duct obstruction
4. History of biliary colic where gall bladder is absent or does not contain stones
5. Palpable stones in the common bile duct
6. Dilatation of the common bile duct
7. Choledochitis
8. Fistula between the biliary and gastrointestinal tracts
9. Operative choledochograph showing filling defects or obstruction
10. Stones in the gall bladder small enough to pass through the cystic duct

RESULTS

A minimum 2-year follow-up was obtained in 95 per cent of the cases, and, on the basis of reports from the patients and their physicians, the number of cases requiring further treatment or reoperation was determined. Excellent results were recorded for 73.4 per cent of the patients. "Excellent" was defined as freedom from any symptom even remotely related to the biliary tract, to the operation, or to a complication of the choledochostomy. Results were classified as "good" in 12.3 per cent of the cases; these cases showed occasional minor gastrointestinal upsets, psychosomatic complaints, or small wound imperfections. Results were not considered "good" in any cases involving reoperation or the subsequent occurrence of jaundice, cholangitis, or cirrhosis. Thus, from the surgeon's standpoint, a satisfactory result was obtained in 85.7 per cent of the 350 patients, a figure similar to the 79 per cent reported by Johnston, Waugh, and Good.[3]

"Poor" results were recorded for 10 per cent of the cases, including those with missed (retained) stones, newly occurring or recurring inflammatory strictures, and those requiring operations for extrabiliary complications after the duct exploration. Also listed in this category were 8 patients who died after discharge from the hospital from causes related to the original disease or to the original operation.

Cases of cholangitis after choledochostomy and cases that required repeat exploration were regarded as representing poor results. A summary of the results of choledochostomy is presented in Table III. Nonfatal complications exclusive of those affecting the biliary system occurred 64 times in a total of 42 patients. The incidence of such complications was 10.8 per 100 operations for exploration of the common bile duct.

TABLE III. RESULTS OF CHOLEDOCHOSTOMY

Excellent	257	73.4%	
Good	43	12.3%	
Total satisfactory			85.7%
Poor			
Cholangitis, re-exploration required, or late death from cause related to primary disease	35	10.0%	
Operative deaths*	15	4.3%	
Total unsatisfactory			14.3%
			100.0%

*From a total of 407 operations including repeat explorations and procedures required to treat nonbiliary surgical complications.

The operative deaths are listed in Table IV according to cause of death and the type of operation that preceded death. The operative mortality in men was 7.3 per cent and in women 2.9 per cent. The reason for this difference was not apparent. The over-all operative mortality was 4.3 per cent for 389 common bile-duct explorations plus the 18 operations required to treat nonbiliary complications.

TABLE IV. OPERATIVE DEATHS

ACCORDING TO PATHOGENESIS		ACCORDING TO TYPE OF OPERATION WHICH PRECEDED DEATH			
			NUMBER	DEATHS	RATE
Hepatic coma	7	Primary choledochostomy	334	8	2.4%
Peritonitis	4	Repeat operation after choledochostomy elsewhere	11	1	9.0%
Myocardial infarct	2	Repeat operation after choledochostomy at University Hospital	44	1	2.3%
Cerebral infarct	1	Operations to treat nonbiliary complications after University Hospital choledochostomy	18	5	28.0%
Hepatic abscess	1	Totals	407	15	4.3%*
Total	15				

*Calculated per 100 patients.

Seven cases in which the patients died in hepatic coma are of special interest. These patients were jaundiced at the time of operation. More significant was the fact that the jaundice had been continuously in evidence for periods of 2 to 12 months before the operation. It is obvious that the operative risk is greatly increased in patients with jaundice of long duration and that the earlier the operation, the less risk will be involved. When the icteric patient is first seen there is often a complacency induced by an incorrect but oftentimes not illogical diagnosis of "medical" jaundice. If vigorous therapy is instituted during the evaluation period, then such a patient has already been prepared for a prompt operation if such becomes indicated.

The preoperative treatment in the presence of jaundice should be intensive but not to a point of diminishing return in terms of the patient's over-all condition. Vitamins are given, with emphasis on C and K. Abnormalities in blood volume are corrected. A high carbohydrate supplement is given to increase hepatic glycogen reserve. In anorectic patients, daily intravenous carbohydrate may be used to supplement oral intake. Metabolic studies in patients with

deficient liver function have indicated the desirability of limiting protein intake to 60 or 70 Gm. per day. The inability of the damaged liver to detoxify and metabolize a heavy and unlimited load of protein breakdown products has been substantiated. It is believed that a detrimental accumulation of ammonia-containing products in the peripheral blood occurs in some of these patients because of faulty protein metabolism in the liver. Experimental evidence has been presented by McDermott, Adams, and Riddell,[4] suggesting that amino-acid oxidase and urease produced by the intestinal bacteria aid in the production of this "meat intoxication." For this reason, bowel sterilization by orally administered neomycin,* or drugs with similar action, has been recommended as preoperative preparation for patients with liver damage.

Patients being operated upon during a prolonged episode of obstructive jaundice should be considered for a simple, temporary drainage procedure if that is anatomically feasible. If definitive correction of the obstructing element can be achieved in a brief operation without a great amount of dissection and blood loss, that should be done. If, however, the operative findings indicate that a prolonged and difficult procedure will be required, it may be well to establish bile drainage as a first stage and then reoperate after a few weeks, when the patient's condition is more likely to permit a successful outcome of the definitive procedure. Prior cholecystectomy often rules out the most satisfactory temporizing procedure, namely, cholecystostomy. In isolated instances where the gall bladder is absent, a dilated intrahepatic duct can be located in the gall bladder fossa by means of aspiration, and a polyethylene catheter can be secured in it for temporary drainage of bile.

POSTOPERATIVE CHOLANGIOGRAPHS SHOWING FILLING DEFECTS

The radiologists reporting on the postoperative cholangiographs in this series have as a rule reported abnormalities as filling defects rather than attempting to differentiate between stones, air bubbles, clots, or mucus. Such caution is desirable. In no instance should repeat exploration be advised on

TABLE V. PATIENTS WITH POSITIVE CHOLANGIOGRAPHS

Shadows vanished		16
No treatment (repeat x-rays negative)	14	
After ether irrigations	2*	
Re-exploration revealing no stones		6
Single film, nonobstructing defects, T tubes removed, asymptomatic since		8
Multiple films, nonobstructing defects, T tubes removed, asymptomatic since		3*
Persistent filling defects, symptoms present, reoperation advised		5*
Persistent filling defects, operative removal of retained stones		12*
Total		50

*Indicates patients regarded as having retained stones.

the basis of a single film. If a constant, potentially obstructing defect is present on several x-ray films made on different days, re-exploration of the duct is advised. Table V shows the results in 50 patients in this series who at one time or another had a cholangiograph interpreted as showing a filling defect.

*Neomycin (Squibb).

In 14 cases, repeat x-rays were normal and the defects on the initial films were concluded to have been artifacts. In 2 cases, ether irrigations after the method of Best, Rasmussen, and Wilson[1] were successful and subsequent films were normal.

In 6 cases in which filling defects appeared on films after the first choledochostomy, repeat explorations were negative. The x-rays after the repeat operation were also negative in each instance. In one of these cases, there was misinterpretation of an artifact on a single film after the initial common bile-duct exploration. There were 2 cases in which it seemed possible that the stones had passed spontaneously in the 3-week interval between the last cholangiograms and the repeat exploration. There were 3 cases with no apparent explanation. Such experience shows that repeated demonstrations of a retained stone should be required with a final cholangiogram on the day before re-exploration.

In 8 patients with single positive x-rays and 3 patients with multiple x-rays positive for filling defects of nonobstructing type, the T tubes were removed and the patients have remained asymptomatic. It was assumed that the 3 patients with multiple positive radiographs had retained small stones which may have subsequently passed through the sphincter of Oddi. Such an explanation is tenable only for as long as such patients remain asymptomatic. Proper dilation of the sphincter of Oddi at the time of duct exploration may permit small solid particles to pass.

There were finally 17 cases with persistently positive x-rays and clinical symptoms of obstruction. In 12 the retained stones have been removed, and repeat exploration has been advised for the remaining 5. Table VI summarizes the cases with stones retained after choledochostomy. In one of the 2 cases that were discovered at autopsy, an impacted stone was found in a secondary duct within the liver, which had not been contributory to death. The second case was that of a patient in whom hypotension had caused the operation to be terminated before it could be completed. The duct had been explored, but the falling blood pressure necessitated omission of the previously planned cholecystectomy. A retained cystic duct stone caused death from a ruptured gall bladder 3 months after the operation. The patient had been asymptomatic until a few days before death.

TABLE VI. PATIENTS WITH RETAINED STONES

Proved by re-exploration and removal	12
Proved by clinical course and repeatedly positive x-rays	8
Shadows disappearing after ether irrigations	2
Retained stones discovered at autopsy	2
	24*

*Incidence of retained stones 6.9 per cent.

DISCUSSION

There are certain recognized absolute indications for common bile-duct exploration. The combination of jaundice, chills, and fever are the most important symptoms indicating the need for duct exploration. Ductal dilatation

and the presence of palpable stones in the duct also indicate that choledochostomy must be performed. There are certain lesser indications in many cases which require careful consideration before duct exploration is omitted. It is to be recognized that the rate of stone recovery in cases with only relative indications for exploration will be considerably lower than in patients having absolute indications for choledochostomy.

The over-all incidence of stones recovered at choledochostomy was 34 per cent. Compared to other published figures indicating higher rates of recovery, it would appear that at this hospital there is a liberal interpretation of the indications for common bile-duct exploration.

Repeat common bile-duct explorations were recorded in 37 cases in this series, 2 operations in each of 27 cases and 3 in each of the other 10. These cases admittedly represent poor results. Three patients chose to have their repeat explorations carried out elsewhere. Due to chronic and recurrent biliary obstruction, several in the group of 37 ultimately suffered from biliary cirrhosis, and for this reason presented nearly prohibitive risks at the time of reoperation. A progressively severe inflammatory stricture had often become the overriding problem, especially in some of those patients requiring a third exploration.

The danger of overlooking stones at the time of duct exploration is greatest in the cases where the surgeon has recovered one or more stones from the duct and assumes that there are no more. Stones were "missed" 7 times as often in duct explorations which were positive for calculi as in those originally considered to have been negative. This liability for error, of course, is not presented by a duct which contains no stones.

As has been shown, excellent results can be achieved in a high percentage of cases. The incidence of recurrent difficulty is usually proportional to the degree of abnormality present at the first operation. From a statistical standpoint, the percentage of good results after choledochostomy has remained nearly constant at the University Hospital during the period from 1934 to 1956.

SUMMARY

At the University of Michigan Hospital, in the period from 1946 to 1956, 350 patients underwent exploratory operations on the common bile duct because of nonmalignant and nontraumatic disease of the biliary tract. The surgical procedures included 389 choledochostomies and 18 operations to treat nonbiliary complications following choledochostomy; the combined operative mortality rate was 4.3 per cent. Mortality was greatly increased in patients with prolonged preoperative jaundice. There was a 6.9 per cent incidence of retained stones after common bile-duct exploration. The hazard of leaving stones in the common bile duct is greatest during a positive exploration in which only a portion of the total number of stones are recovered. As a safeguard, common duct stones should be assumed to be multiple, so that the exploration will not be prematurely ended.

Good or excellent results were achieved in 85.7 per cent of the cases in this series as determined by a nearly complete follow-up of 2 years or more.

REFERENCES

1. Best, R. Russell, Rasmussen, John A., and Wilson, Carlyle E.: An Evaluation of Solutions for Fragmentation and Dissolution of Gallstones and Their Effect on Liver and Ductal Tissue, Ann. Surg. **138**: 570-581, 1953.
2. Buxton, Robert W., and Burk, Lloyd B., Jr.: Choledochotomy, SURGERY **23**: 760-767, 1948.
3. Johnston, Edward V., Waugh, John M., and Good, C. Allen: Residual Stones in the Common Bile Duct: The Question of Operative Cholangiograms, Ann. Surg. **139**: 293-301, 1954.
4. McDermott, Wm. V., Jr., Adams, Raymond D., and Riddell, Athol G.: Ammonia Metabolism in Man, Ann. Surg. **140**: 539-556, 1954.
5. McKittrick, Leland S., and Wilson, Norman J.: Indications for and Results Following Exploration of the Common Bile Duct for Stones, California Med. **71**: 132-137, 1949.
6. Thomson, Frank B.: Residual Stones in the Biliary Ducts, Surg., Gynec. & Obst. 103: 78-84, 1956.

CURRENT CONCEPTS OF THE ANATOMIC, CLINICAL, AND REPARATIVE FEATURES OF FEMORAL HERNIA

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ANATOMIC RELATIONS OF FEMORAL HERNIA

THE femoral ring through which a femoral hernia evaginates is infrainguinal and lies in the interligamentous area between the external iliac vein and the medial lacunar ligament. It differs from the internal ring in that: (1) it has a predilection to dilate in one direction, medialward rather than circumferentially or ovally, (2) it has a triple ligamentous, medial, and anteroposterior boundary and a lateral vascular boundary, with absence of adjacent or surrounding muscle fibers, (3) it is without mobility or contractile function, (4) its weakness is limited chiefly to attenuation or hypoplasia of the lacunar ligament and posterior wall of the inguinal canal, (5) it lies in a horizontal plane with no superimposed muscle to act as an operculum when the abdominal wall is in contraction, (6) the peritoneal sacculation of a femoral hernia is inexplicable on the basis of a vestigial embryonic remnant, and (7) the gubernaculum testis and spermatic cord do not migrate through the femoral ring en route to the scrotum.

A femoral hernia is not of congenital origin unless it is predicated on a preexisting femoral fovea or dilated ring coexisting with deficient substance of the lacunar ligament. This dual conception of the origin of femoral hernia represents the consensus of contemporary views, but it is contrary to the opinion held until a couple of decades ago. In Zimmerman's recent monograph on hernia,[16] the inference is that femoral hernia may be acquired or is congenital, which is interpreted to mean the sac is acquired but the weakness of the medial boundary of the femoral ring is of congenital origin.

Since the posterior boundary of the femoral ring is formed by the underlying superior pubic ramus and inasmuch as the anterior boundary is the inguinal ligament which is generally unyielding, there is little likelihood of anteroposterior dilatation of the ring. Therefore, any expansion of the femoral ring must take place either medially by displacement of the lacunar ligament or laterally by compressing the femoral vein. From repetitive clinical observations it has been found that the latter never occurs. Increasing recognition is being given to the existence of a dual medial structural weakness of the femoral ring: (1) the posterior stratum of the inguinal canal and (2) the base of the lacunar ligament. Anatomic deficits in these structures constitute the principal cause of femoral hernia. Confirmatory of this recent concept, McVay and Anson[12] in 1949 made some interesting observations on cadavers, in which they noted the

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variations in the breadth of the insertion of the posterior wall of the inguinal canal into the posterior iliopubic (Cooper's) ligament. In effect, this relationship is comparable to the arrangement of the anatomic strata which occur in the formation of the conjoined aponeurosis, weakness of which is constantly observed in direct hernia. This deficiency in strength of the posterior wall is traceable to the varying ratio of the fascia transversalis to the aponeurotic and fascicular fibers of the transversus abdominis which play a cardinal role in the development of direct inguinal hernia. Any lack of integrity of this stratum serves as a common denominator for explaining the close association of direct inguinal hernia and femoral hernia which may coexist in 50 per cent of all femoral hernias.[4]

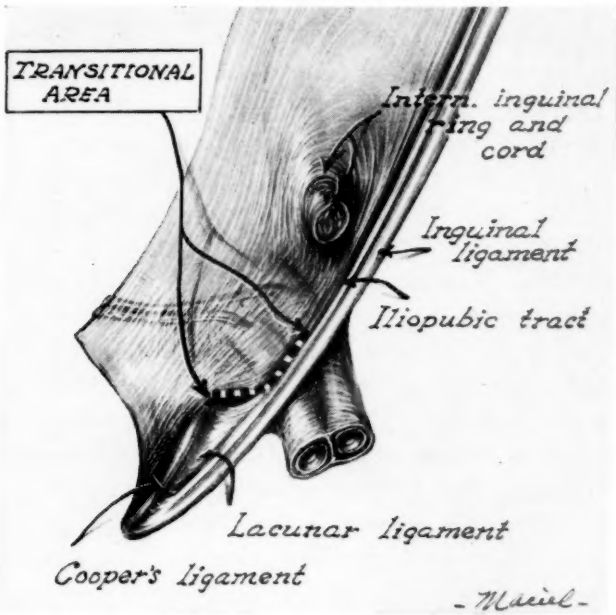

Fig. 1.—Normal anatomy, anterior view.

Direct hernias are prone to occur in the fourth and fifth decades. Similarly, eighty-nine per cent of femoral hernias occur in patients 40 years or older.[9] Although the sac of the femoral hernia is acquired, it must of necessity arise from the peritoneal infundibulum of the inguinopectineal region (Fig. 3, *B*). The following prerequisites occur in varying degrees antedating the development of a femoral hernia: (1) enlargement of the femoral ring, (2) increased ductility of the peritoneum, (3) a yielding structurally weak lacunar ligament and/or posterior wall of the inguinal canal, (4) increased intra-abdominal tension, and (5) pre-existing deficiency of the transitional area.

Transitional Area (Figs. 1 and 2).—The peritoneal locule destined to form a femoral hernia must first traverse a fault in the fascia transversalis and attenuated aponeurosis of the transversus abdominis. The latter form the posterior wall and overlie the femoral ring. This area of potential fascioaponeurotic weakness has been previously designated as the transitional area.[1] Its base is

subjacent to and parallels the inguinal ligament and extends from the lateral margin of the external iliac vessels to the deeply placed Cooper's ligament medial to the iliac vein and femoral ring. In the transvascular portion of the interligamentous space, the posterior boundary of the inguinal canal is not inserted into either the inguinal ligament or Cooper's ligament but into the deep femoral arch which is a part of the iliopubic tract (intermediate iliopubic ligament). Under normal circumstances, the arch is adequate to maintain the integrity of the superjacent mural segment. Nevertheless, repeated clinical observations have shown that the transitional area, which is the most susceptible to herniation, lies medially adjacent to the epigastric vessels. This area is better known as the base of Hesselbach's triangle. Any condition producing a widening of the deep femoral arch, such as dilatation of the femoral ring or narrowing of the insertion of the posterior boundary of the inguinal canal, increases the width of the transitional area and further potentiates its weakness. The variability of the ratio of the aponeurosis of the transversus abdominis to the fascia transversalis of the posterior wall and the variance observed in the width of the insertion of these structural lamina into Cooper's ligament constitute the most constant etiologic denominator found in association with direct inguinal hernia and femoral hernia.

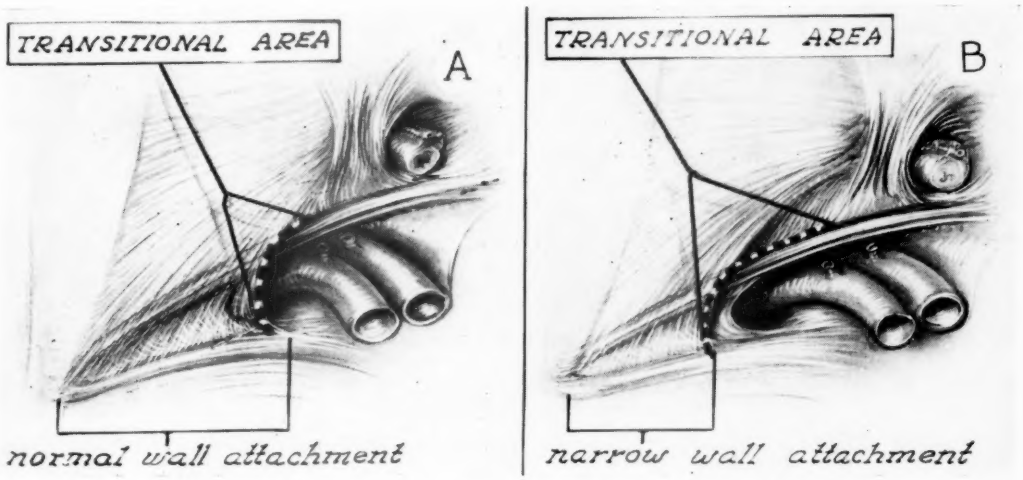

Fig. 2.—Normal anatomy, posterior view.

Formerly a femoral hernia was generally accepted as unilocular, but since we know that the femoral sac arises from the direct inguinal area one might presume that all femoral sacs are bilocular. For instance, when there is a functional weakness of the posterior wall of the inguinal canal, the overlying peritoneum assumes the morphologic contour of the domelike wall which constitutes the basic weakness of a direct hernia (Fig. 3, *D*). When this relationship occurs, a portion of the redundant direct sac with its attenuated coverings derived from the floor of the inguinal canal may be forced through the femoral ring. This is a simple forthright explanation of the dynamics of a direct inguinofemoral hernia. However, there is equally valid explanation for a unilocular femoral hernia (Fig. 3, *C*). If the posterior wall of the inguinal canal remains taut except for the

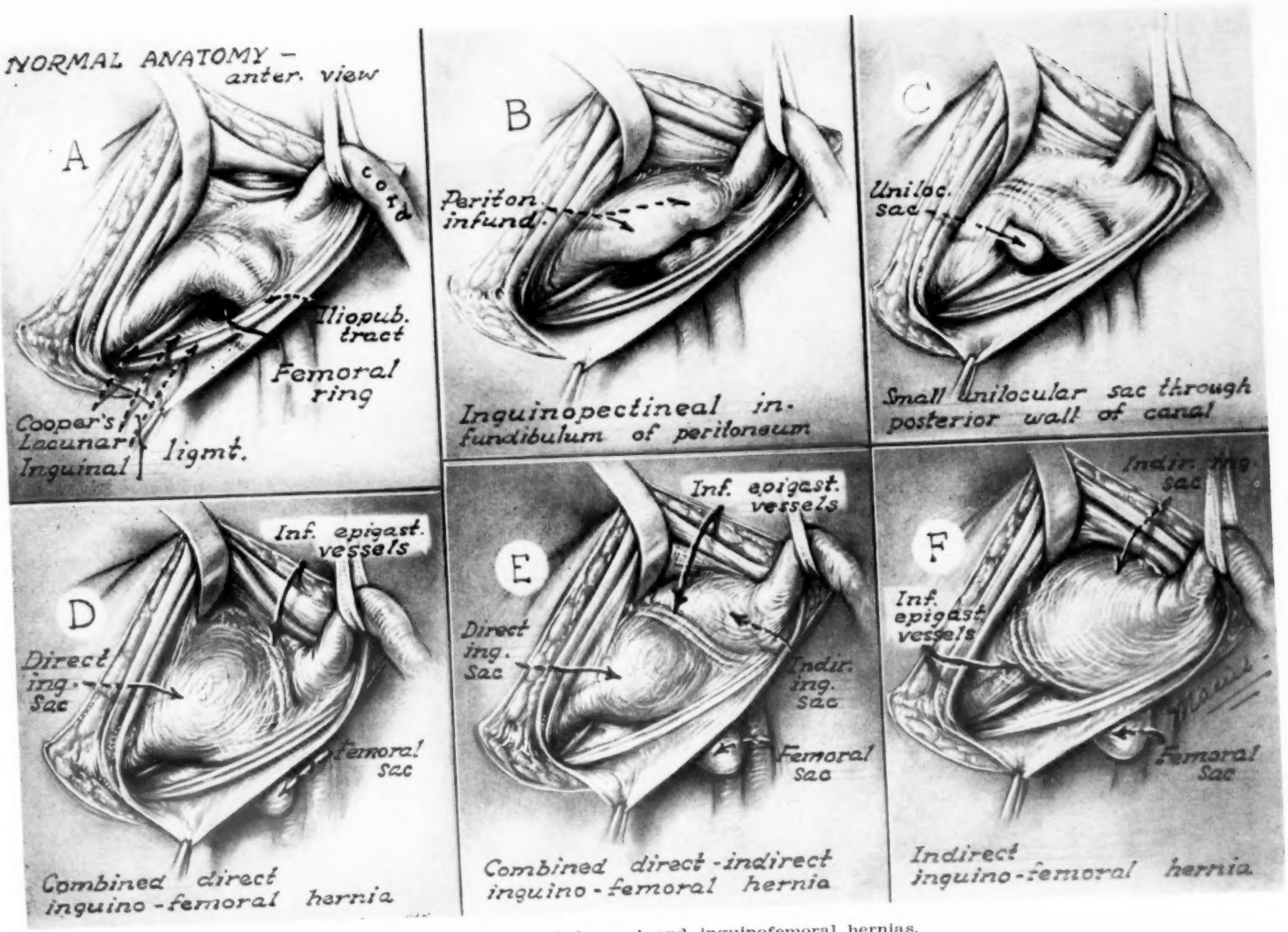

Fig. 3.—Types of femoral and inguinofemoral hernias.

development of a small rent through which the peritoneal sac evaginates, there is no coexisting direct hernia and consequently the sacculation remains a solitary one. Similarly, it is possible for a femoral hernia to spring from the indirect sac (Fig. 3, *F*), but in order to do this the neck of the sac must displace the inferior epigastric vessels and the floor of the inguinal canal medially beyond the level of the femoral ring. When this rare structural distortion occurs the fascia transversalis obviously would not be interposed as a barrier between the indirect sac and the femoral ring.

CLINICAL RELATIONSHIP OF FEMORAL AND INGUINAL HERNIA

Many authorities[4, 8, 9, 12, 14, 15] have recognized the clinical and reparative significance of the coexistence of direct inguinal and femoral hernia (Fig. 3, *E*). McVay and Anson[12] have employed jointly inguinal and femoral hernioplasty in dealing with communicating inguinofemoral sacculations. I have proposed a combined Cooper's and inguinal ligament repair as standard treatment of these closely related inguinal and interligamentous hernias.[1] There are anatomically and clinically valid reasons for approaching every hernia of the inguinofemoral region superiorly, by exposing first the peritoneum at the internal inguinal ring and determining by digital exploration the number and extent of the saccular variants. By consistently following this maneuver of Hoguet,[10] there has been an increase in the number of loculated sacs found in our series. There can be little doubt that before the adoption of this technique many aberrant locules were overlooked in the initial repair. Occasionally a small femoral sac or fovea may be demonstrable which had not been recognized preoperatively.

When a femoral hernia is present it is first inguinalized and then converted into its direct inguinal component. The latter is successively indirectilized and excised high. This technique of retrogressive mobilization of the components of the sac has led to greater appreciation of saccular loculation and has the additional advantage of affording the surgeon the opportunity of palpating the entire posterior wall in evaluating its integrity to determine the type of repair to be used.

Illustrative of the frequency of combined saccular variants, we found in 165 femoral hernias[4] that 82 (49.7 per cent) were unilocular, 50 (30 per cent) had coexisting direct inguinal hernias, and 33 (20 per cent) had combined indirect and direct inguinal components which communicated with the femoral loculation. In reality, 83 (50 per cent) of the femoral hernias in this series were combined inguinofemoral hernias. Recently, Bush,[5] in elaborating on the anatomic variations of the inguina, referred to direct femoral hernia, meaning that the femoral hernia had its origin from the direct component of the inguinal sac. For the sake of clarity and to promote a better understanding of the saccular continuity of the peritoneum of this region, it would seem logical and more objective to employ the term inguinofemoral for those hernias having combined sacs.

As a rule, a femoral hernia is easily recognized. However, occasionally one may have to differentiate a varix, adenitis, lipoma, psoas abscess, properitoneal,

obturator, and Richter's hernia. Only the last three are likely to present diagnostic difficulties. A properitoneal interparietal hernia is an exceedingly rare occurrence. If there is a history of reducible hernia but the pain persists after reduction, the possibility of a properitoneal hernia must be suspected. Pressure over the inguinal ligament in the femoral area will cause pain if a femoral hernia is present; but, because of the superimposed superior pubic ramus, the same maneuver will produce no response from an obturator hernia. Pain radiating down the medial aspect of the thigh to the knee following the distribution of the obturator nerve is perhaps the most characteristic symptom of an obturator hernia.

It should be emphasized that femoral hernia has a high incidence of incarceration and strangulation. McNealy[11] found that 55 per cent of the patients admitted to Cook County Hospital with a diagnosis of femoral hernia had either an incarcerated or strangulated hernia. Incidentally, 40 per cent of these patients had no previous knowledge of the existence of the hernia. This and other confirmatory reports of the high incidence of complications of femoral hernia emphasize the importance of operative correction of all femoral hernias without procrastination.

A Richter's hernia through the femoral ring may be deceptive because of the paucity or inconstancy of symptoms, which vary with the completeness of bowel obstruction. Since only a part of the circumference of the bowel protrudes through the ring, there may be crampy or colickylike pain without abdominal distention, often with nausea or occasionally intermittent vomiting. A mass in the femoral area may be so small that it can be missed on palpation, but there is commonly tenderness to pressure, with a rapid pulse particularly in the elderly patient, in which case one should suspect an occult strangulated femoral hernia. Orr[13] found 0.7 per cent of one per cent of femoral hernias were partial enteroceles, and, according to Foltz,[7] 90 per cent of Richter's hernias are femoral. It is, therefore, of the utmost importance to recognize a femoral hernia, especially if a Richter's type is suspected, since gangrene of the bowel may ensue in 48 hours.

REPARATIVE FEATURES OF INGUINOFEMORAL HERINA

The management of the sac has herein before been dealt with. In the early reparative period of femoral hernia, antedating the turn of the century, efforts were directed toward the correction of what was thought at that time to be the only basic defect, namely, the enlarged femoral ring. Consequently, the ring was either obturated with redundant sac or omentum (Annadale, 1876) or obliterated (Ruggi, 1896) by direct suture of the inferior edge of the inguinal ligament to Cooper's ligament. These reparative measures had only limited success, since the coexisting inguinal weakness had not been recognized and of course was not reinforced at the time of operation. As knowledge of the inguinofemoral, parietal, and saccular relationship became better understood, the reparative techniques were successively modified until a combined inguinofemoral repair has been adopted by many contemporary surgeons. In brief, the first

step of the combined repair consists in attaching the fascioaponeurotic margins of the posterior boundary of the inguinal canal to Cooper's ligament (Fig. 4). This maneuver excludes the femoral ring and the interligamentous space. The cut edge of the inguinal ligament is next turned down and attached to the superior margin of Cooper's ligament, which reinforces and bridges the interligamentous space. The third dimension of the repair is attained by suturing the adjacent converging walls created by the preceding maneuvers. The latter step synthesizes the conjoined walls and further augments the repair.

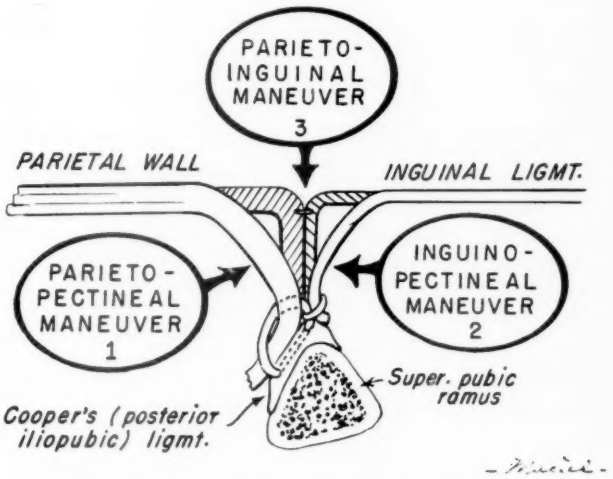

Fig. 4.—Tridimensional repair.

Strategically, one might think the three-dimensional repair would be invulnerable. After considerable experience with this technique, it, too, has been found to have certain pitfalls. In over 1,200 combined repairs performed in our clinic, there has been a progressive lowering of the recurrence rate. Nevertheless, two types of recurrences have been observed. One occurs in the notoriously weak transvascular area, which is usually small and often unrecognized by the patient; in the other, Cooper's ligament has been peeled from its normal attachment to the superior pubic ramus by injudicious placement of sutures and/or by increased intra-abdominal pressure. The latter is characterized by a large eventration hernia, since there is no resistant posterior wall. The latter is prone to occur within a few weeks or months after repair. On examination no resistant floor is felt because it has no solid anchorage. At reoperation of three of the latter type of hernia which we have observed, it was found that Cooper's ligament had become detached for some distance leaving a smooth shiny superior pubic ramus. To correct such a hernia the combined parietal wall is reattached to the superior pubic ramus, using fascial sutures which are passed through holes made in the underlying bone. In those 3 cases the walls have remained secure.

While the inferior approach to an uncomplicated femoral hernia is obsolete, it still has a place, and I would not advocate its complete abandonment. For instance, it is conceivable that a simple cutaneous enterostomy in a moribund patient with a strangulated hernia and probable gangrenous bowel may be fully

justified. If the patient survives, the continuity of the bowel may be subsequently restored. Orr[13] reported a case with a strangulated Richter's femoral hernia which developed an abscess and was successfully drained. These were obviously lifesaving measures and the repair of the hernia rightly was relegated to a subsequent time. Where strangulation of bowel is suspected, the vertical or T incision proposed by Dennis and Varco[6] affords a safe approach and is adequate for resection and end-to-end anastomosis.

DISCUSSION

With increasing knowledge of the correlative relationship in the sequential development of the sacculations of the inguinofemoral region, there have been successive changes in the reparative techniques to meet these challenges. For instance, by routinely practicing methods which give more complete exposure of the inguinopectineal area, multilocular sacs are found with increasing frequency. This is attributable to better visualization of the composite region, making it possible to ferret out and demonstrate formerly unrecognized dormant weaknesses of the parietal wall. The superior or inguinal approach enables surgeons to palpate the posterior wall and to determine more accurately its integrity.

Statistically, it has been shown that one-half of all femoral hernias[4] have combined communicating sacs. Therefore, the presence of a femoral hernia should arouse the suspicion that a direct inguinal component exists and communicates with it, although the latter may not be demonstrable preoperatively. This cumulative knowledge is advantageous in enabling the surgeon to be better prepared to deal effectively with all potential weaknesses.

The key to a fuller understanding of femoral and inguinofemoral hernias is the recognition of the clinical and anatomic perspective of the transitional area. This area represents the change in the insertion of the fascia transversalis from the lateral recurved portion of the inguinal ligament to the iliopubic tract and medially to the more deeply placed Cooper's ligament. The normal width of the transitional area corresponds to the femoral arch. Any narrowing of the insertion of the posterior boundary of the inguinal canal has the effect of widening the transitional area. The more attenuated and wider this zone the greater its potential vulnerability to herniation. By the same analogy, this congenital and/or acquired anatomic deficit of the transitional area presents a concomitantly greater challenge to the creation of a firmly anchored wall.

The introduction of the combined repair is a milestone in the progress of hernia repair. However, it is incumbent on the surgeon through cumulative experience to evaluate the posterior boundary of the inguinal canal and decide the most feasible method of repair. If Cooper's ligament is friable or attenuated, which is rare, it would be inviting recurrence to employ it. Of paramount importance is the secure anchorage of the triple parietal strata. If one is confronted with an inadequate Cooper's ligament, the placement of fascial sutures through the conjoined strata and through 3 or 4 holes made in the pubic ramus may be the most feasible means of attaining a firmly anchored wall.

SUMMARY

1. A broader concept of femoral hernia has been emphasized.

2. An anatomic comparison of the internal inguinal ring and the femoral ring has been done.

3. The saccular relationship of femoral hernia versus direct-indirect inguinal hernia has been elaborated upon.

4. The transitional area has been more accurately defined anatomically and its etiologic relationship to the primary mural weakness in the development of femoral or direct inguinofemoral hernia has been stressed.

5. The clinical significance of femoral hernia and its potentiality for strangulation should be appreciated by the physician and surgeon alike.

6. The combined inguinal ligament and Cooper's ligament repair is the most reliable operative procedure that is presently available for inguinofemoral hernia.

REFERENCES

1. Burton, Claud C.: Collective Review; Inguinopectineal Hernias—Classification and Correlation (Internat. Abstr. Surg.) Surg., Gynec. & Obst. **97**: 417-431, 1953.
2. Burton, Claud C.: Collective Review; Rationale and Factors for Consideration in Cooper's Ligament Hernioplasty (Internat. Abstr. Surg.) Surg., Gynec. & Obst. **85**: 1-8, 1947.
3. Burton, Claud C.: The Combined Cooper's Ligament and Inguinal Ligament Hernia Repair, Surg., Gynec. & Obst. **98**: 153-160, 1954.
4. Burton, Claud C., and Bauer, Robert A., Jr.: Femoral Hernia: a Review of 165 Repairs, Ann. Surg. Accepted for publication.
5. Bush, E. A.: Some Anatomic Observations in the Inguinal Region, Am. Surgeon **23**: 911, 1957.
6. Dennis, C., and Varco, R. L.: Femoral Hernia With Gangrenous Bowel, SURGERY **22**: 312, 1947.
7. Foltz, E. L.: Richter's Hernia; Three Case Reports, Univ. Hosp. Bull. Ann Arbor **13**: 105, 1947.
8. Fratkin, L. B.: Femoral Hernia Following Inguinal Herniorrhaphy, Canad. M. A. J. **58**: 365, 1948.
9. Hagan, W. H., and Rhoads, J. E.: Inguinal and Femoral Hernias; a Follow-Up Study, Surg., Gynec. & Obst. **96**: 226, 1953.
10. Hoguet, Joseph Pierre: Direct Inguinal Hernia, Ann. Surg. **72**: 671-674, 1920.
11. McNealy, R. W., Lichtenstein, M. E., and Todd, M. A.: Diagnosis and Management of Incarcerated and Strangulated Femoral Hernia, Surg., Gynec. & Obst. **74**: 1005, 1942.
12. McVay, C. B., and Anson, B. J.: Inguinal and Femoral Hernioplasty, Surg., Gynec. & Obst. **88**: 473, 1949.
13. Orr, T. G., Jr.: Richter's Hernia, Surg., Gynec. & Obst. **91**: 705, 1950.
14. Telle, L. D.: Inguinal and Femoral Hernia; a Review of 1,694 Cases, Am. J. Surg. **93**: 433, 1957.
15. Wilmoth, C. L.: Femoral Hernia in the Male, Ann. Surg. **105**: 549, 1937.
16. Zimmerman, L. M., and Anson, B. J.: Anatomy and Surgery of Hernia, Baltimore, 1953, Williams and Wilkins Company, p. 238.

THE FEASIBILITY OF INVESTIGATING THE EFFECT OF LOCAL MEDICATION ON BURN HEALING

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INTRODUCTION

IT IS understandable that the medical profession greets each new panacea for the local treatment of burns with something less than unrestrained enthusiasm. Although testimonials concerning the efficacy of various ointments and oils are readily available, no preparation has so far been demonstrated to promote healing. When some medication or bland ointment is applied to a burned area it is done with the intention of alleviating pain or of decreasing mechanical abrasion from a dressing. It is hoped that the treatment will do no harm and, if the agent used possesses some antibacterial property, that it might lessen the chance of infection. Even with meddlesome care a mild burn usually heals rapidly and completely, and for centuries this restorative power of nature has been attributed to one preparation or another. When the full thickness of the skin is injured in such a way that all epithelial elements are lost, repair will proceed slowly from the undamaged periphery. Claims that a medication promotes the epithelial repair of a third-degree burn without subsequent scarring make little sense; it would as likely restore an amputated limb. Such testimonials quite naturally produce skepticism concerning the other supposed attributes of the product.

Over the years we have been asked to test many compounds, some reasonable and others bizarre, to determine their effect upon the healing of burns. These requests have always been declined because our experimental methods did not lend themselves particularly well to this type of procedure and we were much more interested in exploring the factors which govern burn severity. However, as our methods and experimental designs became more refined, we began to wonder about the feasibility of evaluating local therapeutic agents in the laboratory.

By using the same total exposure and exposure time with the modified carbon arc searchlight, it is possible to produce many similar burns. Comparison of the extent of epithelial coverage of treated and untreated lesions at a selected time after injury might then give an indication of any markedly beneficial or deleterious effect of a medication. This report records our study of 5 medications by this type of experiment.

MATERIALS AND METHODS

Young Chester White pigs, anesthetized with intraperitoneal Dial with urethane (Ciba), were used as the experimental animals because their skin

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resembles human skin in thickness and composition and reacts similarly to thermal injury.[4, 5] Surface contamination does not lead to infection of small burns on pigs. It is, therefore, possible to evaluate the direct effect of medication on epithelial coverage without regard to a secondary effect due to suppression of infection. Since the animals, anesthetized at the time of injury, show no evidence of pain on awakening, whether treated or not, pain relief from medication cannot be observed.

Evaluation of the following preparations was requested by their manufacturers or distributors:

1. *Salcolan ointment*, manufactured by the Rich Company, Inc., Houston, Texas. Content: cod liver oil, lanolin, caraway oil, olive oil, and phenyl salicylate.
2. *Skincuo*, an ointment prepared for Vincent Viscuso, 414½ W. 5th Ave., McKeesport, Pennsylvania. Content: mineral oil, cente herbe, sulfur, boric oxide and so forth.
3. *Epital*, made and supplied by A. Farkas, Chemical Research Laboratories, 425 NE 173rd St., North Miami Beach, Florida. Described as "a glucosid type compound, composed of carbon, hydrogen and oxygen only," obtained from plants of the *Liliacea* family.

In addition to these 3, two other medications were studied. Furacin (Eaton Laboratories) was chosen because it is commonly used as a dressing for burns. Perazil 2 per cent (Burroughs Wellcome and Company) was selected as representative of a water-soluble antihistamine cream.

The heat source was a modified army carbon arc searchlight.[1, 2] All burns were produced by the delivery of 10 calories per square centimeter during a 3-second exposure time. In earlier experiments[6] it had been found that most burns resulting from this thermal dose will be of moderate second-degree severity. In addition, it had been determined that, although all are covered by new epithelium 14 days after injury, half or more are not completely covered 9 days after burning. The size of the burns was controlled by a port 1.7 cm. in diameter.

Twenty-four burns were placed on the sides of each of 3 animals. Of the 24, four exposure sites were not treated and four were treated with each of the 5 selected medications. The 72 burns in this part of the experiment were randomized in such a way that there was equal probability of any one site being untreated or treated with any of the 5 ointments or creams. On each of 5 additional animals, 20 burns were produced. Half of the burns on each animal were treated with one of the medications, the other half were left untreated. Randomization assured equal probability of any one exposure site on a given animal being treated or untreated; in these 5 animals, comparable sites were treated with the different medications and comparable sites were left untreated. On all animals, treatment consisted of the application of the ointment once a day, beginning with the day of injury, for 5 days. On the ninth day after injury, after 4 days without treatment, each burn was biopsied

in such a way that normal tissue was included on each side of the healing lesion. The tissues were placed in 10 per cent formalin and sections were stained by a method for the differentiation of burned and normal tissues.[3]

On microscopic examination of the sections it was noted whether or not new epithelium completely covered the tissue beneath the slough, or whether coverage was far advanced, moderately advanced, or very incomplete.

RESULTS

The results are summarized in Tables I, II, III, and IV which are arranged so that the following comparisons can be made: (1) the effect of each treatment versus no treatment, (2) the rates of healing in different animals, and (3) the influence of the sites of the burns on the rate of epithelial coverage.

Table I shows the degree of epithelial coverage of the burns on the 3 pigs on which the sites of injury were treated by one of the 5 medications or were not treated. This table, by itself, would seem to indicate the superiority of no treatment since only 2 of 12 such burns showed very incomplete coverage while at least half of each group of treated burns showed poor epithelization. Again, if this table alone is considered, Perazil, for example, would seem to have a deleterious effect. Table II, which gives the results on the 5 animals,

TABLE I. EPITHELIAL COVERAGE NINE DAYS AFTER PRODUCTION OF MODERATE SECOND-DEGREE BURNS—RESULTS IN THREE ANIMALS IN WHICH ALL FIVE OINTMENTS WERE TESTED

TREATMENT	NUMBER OF BURNS SHOWING			
	COMPLETE EPITHELIAL COVERAGE	FAR-ADVANCED COVERAGE	MODERATELY ADVANCED COVERAGE	VERY INCOMPLETE COVERAGE
None	2	3	6	2
Skincuo	0	2	3	7
Salcolan	3	1	0	8
Epital	1	3	2	6
Furacin	1	0	5	6
Perazil	0	0	4	8

TABLE II. EPITHELIAL COVERAGE NINE DAYS AFTER PRODUCTION OF MODERATE SECOND-DEGREE BURNS—RESULTS IN FIVE ANIMALS IN EACH OF WHICH A DIFFERENT OINTMENT WAS TESTED

TREATMENT	NUMBER OF BURNS SHOWING			
	COMPLETE EPITHELIAL COVERAGE	FAR-ADVANCED COVERAGE	MODERATELY ADVANCED COVERAGE	VERY INCOMPLETE COVERAGE
Skincuo	0	1	0	9
None	0	0	1	9
Salcolan	0	0	3	7
None	1	0	0	9
Epital	1	0	0	9
None	0	2	2	6
Furacin	0	0	1	9
None	1	0	2	7
Perazil	5	4	1	0
None	3	4	3	0

each of which had half its burns treated with one of the preparations and the other half left untreated, conveys a different impression. If the untreated burns in these 5 pigs are considered, a variation in the rate of epithelization from animal to animal can be seen. In the pig treated with Perazil, none of the untreated burns shows a delay in coverage, while in the others from half to three-fourths of the 12 have very incomplete epithelial coverage. Comparison of each group of treated and control burns fails to demonstrate either definite benefit or harm from any of the treatments.

Tables III and IV illustrate an effect of the anatomic location of a burn on its rate of epithelial coverage. Row A consisted of 5 or 6 burns along the side of the animal about 2 inches ventral to its spine. Row B contained 5 or 6 burns located about 3 inches nearer the belly. Whether treated or not, the burns in the dorsal row tended to show more advanced epithelial regeneration than did the ones in the ventral row. It can also be seen that none of the treatments hastened epithelial coverage in the more sluggish Row B. Likewise, no treatment definitely enhanced or delayed healing in the Row A burns. The seemingly harmful effect of some medications shown by the data in Table I is probably due to the anatomic distribution of burns treated by these preparations (Table III).

TABLE III. CONTRAST IN HEALING RATES OF BURNS IN DORSAL AND VENTRAL ROWS
(Same animals as Those in Table I)

TREATMENT	NUMBER OF BURNS SHOWING			
	COMPLETE EPITHELIAL COVERAGE	FAR-ADVANCED COVERAGE	MODERATELY ADVANCED COVERAGE	VERY INCOMPLETE COVERAGE
Skincuo				
Row A*	0	2	2	3
Row B†	0	0	1	4
Salcolan				
Row A	3	0	0	2
Row B	0	1	0	6
Epital				
Row A	1	2	0	3
Row B	0	1	2	3
Furacin				
Row A	1	0	1	2
Row B	0	0	4	4
Perazil				
Row A	0	0	2	2
Row B	0	0	2	6
None				
Row A	1	2	4	2
Row B	1	1	1	0

*Row A—Nearer the spine.
†Row B—Nearer the belly.

DISCUSSION

It is well to point out the limitations of this type of experiment as an evaluation of the local treatment of burns. Possible benefits from the alleviation of pain and the prevention of secondary infection cannot be assessed in

TABLE IV. CONTRAST IN HEALING RATES OF BURNS IN DORSAL AND VENTRAL ROWS
(Same Animals as Those in Table II)

TREATMENT	NUMBER OF BURNS SHOWING			
	COMPLETE EPITHELIAL COVERAGE	FAR-ADVANCED COVERAGE	MODERATELY ADVANCED COVERAGE	VERY INCOMPLETE COVERAGE
Skincuo				
Row A*	0	1	0	4
Row B†	0	0	0	5
None				
Row A	0	0	1	4
Row B	0	0	0	5
Salcolan				
Row A	0	0	2	3
Row B	0	0	1	4
None				
Row A	1	0	0	4
Row B	0	0	0	5
Epital				
Row A	0	0	3	2
Row B	1	0	0	4
None				
Row A	0	1	1	3
Row B	0	1	1	3
Furacin				
Row A	0	0	1	4
Row B	0	0	0	5
None				
Row A	1	0	2	2
Row B	0	0	0	5
Perazil				
Row A	3	2	0	0
Row B	2	2	1	0
None				
Row A	2	2	1	0
Row B	1	2	2	0

*Row A—Nearer the spine.
†Row B—Nearer the belly.

this way. Since small, partial thickness burns heal rapidly even under adverse circumstances, it is difficult to detect any but the gravest deleterious effects of treatment. Only striking benefit or harm from a medication would become obvious. Neither effect was seen in this study.

The natural variations in healing rates from animal to animal and from one site to another on the same animal, demonstrated well by this experiment, make clear certain pitfalls to be avoided in attempting an experimental assessment of local treatment for burns. If different animals are used for each treatment, only marked differences should be seriously considered. If different medications are tested on different injury sites on the same animal, the effect of location of the lesion must be carefully evaluated.

It is probable that the velocity of the healing process is maximal under ordinary circumstances. There has never been any proof that it could be consistently accelerated. Infection, drying, or therapeutic agents may retard it. The question at issue is often not how much a medication speeds healing but rather how much it delays repair in return for the comfort or satisfaction it gives.

The kindness of nature in providing us with a mechanism for the rapid repair of minor injuries will continue to lead, just as it has in the past, to extravagant praise for various burn ointments, oils, lotions, and creams. This is regrettable only in that if a truly beneficial preparation is ever discovered (or if it is now available to us) our ears, long accustomed to so many misleading claims, will be nearly deaf. In selecting a preparation for the local treatment of a minor burn, there are many from which to choose. Most do no great harm, many add to the comfort of the patient, and some may decrease the chance of infection. The acceptance of these preparations for the treatment of small burns should not mean that they are also to be used when a larger area of the body has been injured. Here, only a treatment which has been demonstrated to have no toxic effect can be permitted.

Our primary objective, the use of carefully controlled laboratory experiments for judging the effect of locally applied agents on the healing of burns, has been accomplished. However, it should be clearly understood that such a method evaluates the healing process alone and does not give insight into the many ancillary factors which may result when patients are treated by the application of some impressive-looking substance.

SUMMARY AND CONCLUSIONS

1. The possibility of evaluating, on experimental animals, the effects of different medications on the rate of burn healing was explored. The method used was satisfactory for the detection of differences in epithelial recovery, but it gave no indication of analgesic or antiseptic properties.

2. Five ointments were tested for their efficacy in the treatment of small, moderate second-degree burns. None was found to promote or delay healing to a significant degree.

3. Variations in the rates of epithelial regeneration from animal to animal and from one site of injury to another on the same animal were noted. The necessity of considering these variations in any attempt to assess local burn therapy is discussed.

4. The fact that a medication may do no noticeable harm when used on a small burn does not imply that it is equally innocuous when applied to a larger injured area.

REFERENCES

1. Davis, T. P., Krolak, L. J., Blakney, R. M., and Pearse, H. E.: Modification of the Carbon Arc Searchlight for Producing Experimental Flash Burns, J.O.S.A. **44**: 766-769, 1954.
2. Davis, T. P., and Pearse, H. E.: The Use of the Carbon Arc and Burning Magnesium as Thermal Sources for Experimental Burns, Ann. Surg. In Press, 1958.
3. Hinshaw, J. R., and Pearse, H. E.: Histologic Techniques for the Differential Staining of Burned and Normal Tissues, Surg., Gynec. and Obst. **103**: 726-730, 1956.
4. Moritz, A. R.: Studies of Thermal Injury. III. The Pathology and Pathogenesis of Cutaneous Burns, An Experimental Study, Am. J. Path. **23**: 915-941, 1947.
5. Moritz, A. R., and Henriques, F. C.: Studies of Thermal Injury. II. The Relative Importance of Time and Surface Temperature in the Causation of Cutaneous Burns, Am. J. Path. **23**: 695-720, 1947.
6. Payne, F. W., and Hinshaw, J. R.: Histologic Studies of the Early Healing Process in Moderate Second Degree Burns, Univ. of Roch. Atomic Energy Project Report, *UR-514*, 1958.

A SIMPLE EXTRACORPOREAL DEVICE FOR REDUCING ELEVATED BLOOD AMMONIA LEVELS

Preliminary Report

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AN ELEVATED level of ammonia in the circulating blood is considered by many investigators to be a cause of the neurologic syndrome of hepatic coma. Nitrogenous substances may precipitate such a crisis in susceptible subjects with either spontaneous or surgically constructed portal-systemic shunts.[8, 17]

Increased concentrations of ammonia have been reported in citrated blood.[6, 16] In an investigation of the biochemical alterations which occur during the storage of whole blood, we made similar observations and found that ammonia increased irrespective of the method of collection or preservation of the blood.[11] Passage of the blood through an ion-exchange resin reduced this high level of ammonia to a normal range in all instances.[12] Limited studies to determine whether the in vitro removal of ammonia by resins could be duplicated in experimental animals have shown sufficient promise to warrant a preliminary report of this simple technique.

MATERIALS AND METHODS

The cation-exchange resin employed was Dowex 50-X8, sodium cycle, in sterile columns 12 cm. long and 3½ cm. wide, each containing 50 Gm. of resin. The column casing and tubing consisted of the hemorepellent plastic, Vinylite.†

Several possible devices were designed; two were eventually selected because of greatest simplicity. One of these is shown in Fig. 1. The other was essentially the same unit but without the collection chamber. They are referred to hereafter as models A and B.

Two groups of animals were used. In the first group, 3 adult mongrel dogs with normal blood ammonia levels were anesthestized with intravenous sodium Pentothal. A femoral artery and vein were exposed and cannulated. Two animals were perfused with model A and one with model B. The period of perfusion was 30 minutes in each case, and thereafter recovery from anesthesia was uniformly prompt.

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*Post-doctorate Research Fellow, National Institutes of Health.

†The component parts are available commercially from Fenwal Laboratories, Somerville, N. J.

In the second group, acute hepatic ischemia was produced in 2 dogs by creating an Eck fistula and ligating the hepatic artery in one stage. These animals never recovered from anesthesia and were in profound coma within 3 hours. Hemoperfusion in these dogs was started when serial determinations revealed the blood ammonia level to persist above 500 mcg. per cent. Heparin sodium, 1.5 mg. per kilogram of body weight, was administered intravenously. The afferent tubing was inserted into a femoral artery, and the efferent one into the femoral vein of the opposite extremity. One dog was connected with model A and, as in the first group, the resin columns were not changed during perfusion. The second dog was connected with model B and 2 fresh columns were used after each 500 ml. of perfusion. Ten ml. of 10 per cent calcium gluconate was given intravenously at the conclusion of perfusion to partially compensate for calcium removed.

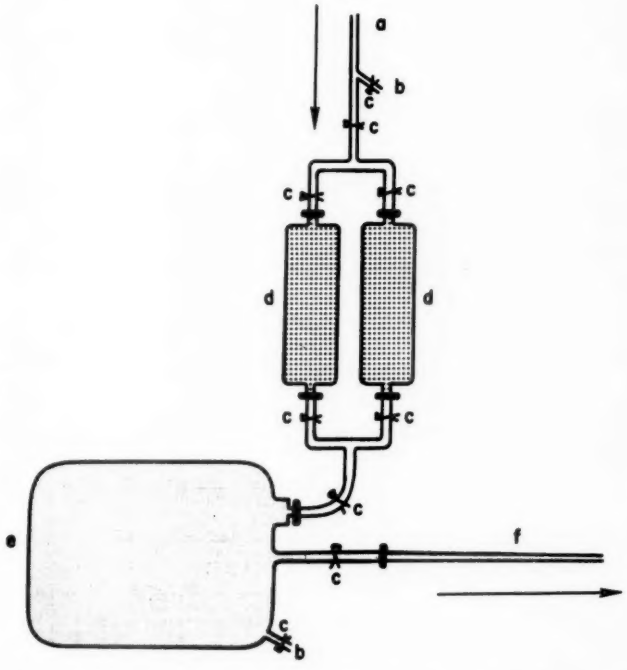

Fig. 1.—Diagram of perfusion columns, model B. *a*, Afferent limb; *b*, side-arms for sampling; *c*, clamps; *d*, resin columns; *e*, plastic container of 150 ml. capacity; *f*, efferent limb. Model A differs from the above only in that the plastic container is excluded from the unit.

Blood samples drawn from the influent limb of the device were analyzed chemically. Blood ammonia was determined in duplicate by the method of Seligson.[14] Sodium and potassium were analyzed by internal flame photometry.

RESULTS

All 3 normal dogs were closely observed for 48 hours after perfusion and showed no signs of any deleterious effects from the procedure. There was an average 55 per cent reduction in the ammonia blood level at the conclusion of the perfusion in these dogs.

The results obtained in the dogs with acute ischemia are presented graphically in Figs. 2 and 3. In the dog on model A the ammonia decreased from 769 to 537 mcg. per cent in 5 minutes and to 307 mcg. per cent in 30 minutes. Over the entire period the potassium decreased gradually from 3.39 to 2.38 mEq. per liter, and sodium increased from 130 to 140 mEq. per liter. The use of model B in the second dog allowed the blood flow through the resin

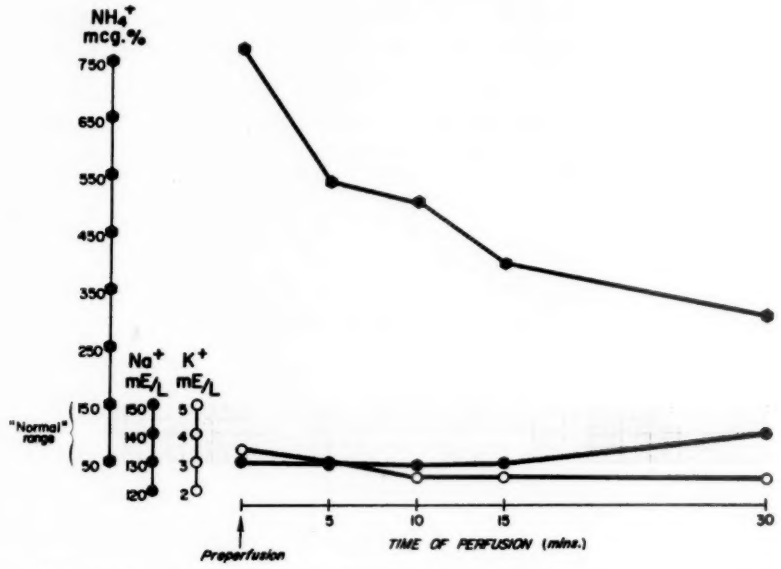

Fig. 2.—Electrolyte studies on dog with acute hepatic ischemia connected to model A. (mE/L = mEq./L.)

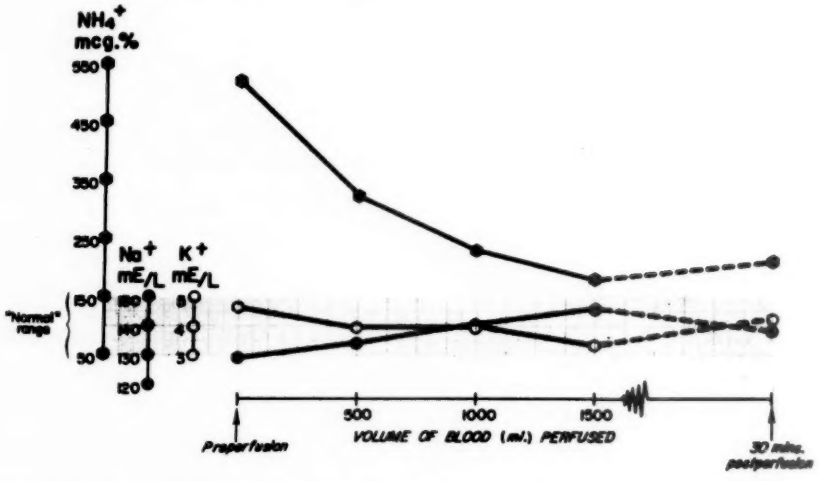

Fig. 3.—Electrolyte studies on dog with acute hepatic ischemia connected to model B. (mE/L = mEq./L.)

columns to be measured. As mentioned above, fresh columns were substituted after each 500 ml. of perfusion. More columns in series or parallel were not employed in order to keep the device compact and to avoid excessive pooling of blood outside the body. The ammonia level again fell precipitously from

520 to 320 mcg. per cent but in this case continued to decrease to 180 mcg. per cent after perfusion of 1,500 ml. of blood. The potassium gradually decreased from 4.65 to 3.30 mEq. per liter, while the sodium increased from 127.5 to 146 mEq. per liter. One-half hour after the perfusion was discontinued the sodium and potassium had begun to return to preperfusion levels, and the blood ammonia level had begun to rise again.

DISCUSSION

The treatment of hyperammoniemia at present includes the administration of glutamate and arginine.[1, 9] The efficacy of these agents is still controversial. In other laboratories, efforts have been made to develop an apparatus to extract excess ammonia from the circulating blood. Kiley, Welch, Pender, and Welch[7] reported that, in experimental animals with "meat intoxication syndrome," the blood ammonia concentration was lowered 50 per cent by employing a Kolff-type artificial kidney. The time of hemodialysis was 3 hours, and 100 L. of bath fluid was used. A more recent communication by Otto and his co-workers[10] from the same laboratory described an average blood ammonia extraction of 85 per cent by an isolated homologous liver perfused with arterial blood using gravity flow. Our initial results obtained with a much simpler device are comparable with these reported figures.

Dock[2] about one decade ago, first suggested the use of ion-exchange resins in hypernatremic states. The literature is replete with reports on the application of these substances to remove sodium or potassium but records no instances of their having been employed previously by hemoperfusion for the removal of ammonia. Parenthetically, it may be mentioned that there have been reports of orally administered ammonium-containing resins precipitating prehepatic coma in patients with portal cirrhosis.[5, 15]

To date, we have had the opportunity to apply this device to one patient. We were limited technically in the performance of hemoperfusion, but the remarkable clinical change following the procedure justifies inclusion of this case history in this report.

CASE REPORT

A 39-year-old woman with metastases to the liver from a cervical carcinoma was seen by us shortly after developing repeated episodes of "flapping" tremors and convulsions alternating with deep stupor. Since the clinical picture was consistent with hepatogenic encephalopathy, a blood specimen was analyzed for ammonia and yielded a value of 822 mcg. per cent, one of the highest values encountered by us in a patient.

Because of her disoriented state it was not possible to draw blood by a satisfactory venipuncture. Therefore, a Cournand needle was inserted in the brachial artery; blood was withdrawn for passage through resin columns arranged as in model B and returned to the patient via the contralateral median basilic vein. A total of 4 resin columns was employed. The patient's prothrombin level, unlike the other hepatic function tests, was normal. Heparin was not used, however, because of the possibility of hemorrhage from her fungating, ulcerated cervical tumor. Clotting occurred in the afferent tubing after slightly more than 1,000 ml. of blood had been perfused, and the procedure was discontinued after a perfusion of 35 minutes. After perfusion of 500 ml. of blood, the ammonia concentration fell to 718 mcg. per cent. After perfusion of 1,000 ml., it fell to 637 mcg. per cent, a net decrease of approximately 20 per cent. Sodium and potassium levels were unchanged.

Notwithstanding what seemed an inadequate trial, we were amazed to observe a complete remission of the patient's symptoms. She ceased to convulse, became lucid within one hour of the procedure, and 8 hours later was alert, sitting up in bed, and smoking a cigarette. Unfortunately, no determinations of blood ammonia were made during the immediate postperfusion interval. Thirty hours after the procedure, however, the level was 77 mcg. per cent. At the time of this writing, 3 weeks later, the patient is mentally alert, has incurred no further convulsions or relapses into coma, and is being treated with a low-protein diet and tetracycline.

It is difficult to define the exact role which only partial reduction in hyperammoniemia had in clearing the patient's symptoms. It may be speculated that her threshold of neuro-excitability was so high that even 20 per cent lowering of blood ammonia was sufficient to reverse the clinical picture, 600 mcg. per cent apparently having been the critical neurotoxic level in the patient. Applicability of the procedure to the bedside is suggested by this case.

DISCUSSION

Dowex 50-X8, Na^+ is a sulfonated polysterene divinyl benzene copolymer. It sequesters ions such as calcium, potassium, magnesium, and ammonium in exchange for sodium. Replacement of these electrolytes may be required because of disturbances attendant upon deficiencies in calcium, potassium, and magnesium.[3, 4, 18] The potential hazard of increased sodium is probably not as serious. Most patients with advanced hepatic damage exhibit hyponatremia,[13] and other forms of treatment, such as glutamate therapy, supply larger amounts of sodium on a milliequivalent basis.

Without delving into the physicochemical complexities of resin exchanges, it may be stated that with the number of divinyl benzene cross-linkages which Dowex 50-X8 possesses there is greater affinity for potassium than for ammonium. By varying the number of cross-linkages, a resin manfesting greater ionic selectivity for ammonium over other radicals may be prepared. Studies are under way on several resins in an effort to obtained one tailor-made for this purpose. Ultimately, such a resin will require intensive study to determine what influence it may have on platelets and other hemic constituents, including factors essential to coagulation. A device containing resin extracting mainly ammonium would in this capacity, function as an "artificial liver."

Although we have observed no untoward effects in the subjects investigated, the afore-mentioned represent some of the questions which will require elucidation before safe clinical hemoperfusion through resins may be achieved. We are currently testing the technique in Eck fistula dogs for reversal of ammonia-induced neurotoxicity and improved longevity after production of gradual hepatic ischemia. This preliminary report is presented in the hope that it will stimulate others to investigate this method which offers promise of a safe and simple treatment of hyperammoniemia.

SUMMARY

1. Preliminary experiences in the use of a cation-exchange resin for lowering elevated blood ammonia levels are presented.

2. Hemoperfusion through resin columns resulted in no deleterious effects in 3 normal dogs.

3. High blood ammonia levels resulting from surgically induced acute hepatic ischemia were markedly lowered in 2 dogs following hemoperfusion through cation-exchange resin columns.

4. A reduction of hyperammoniemia by this method with subsequent remission of symptoms in one patient in hepatic coma is reported.

REFERENCES

1. Bessman, S. P., Shear, S., and Fitzgerald, J.: Effect of Arginine and Glutamate on Removal of Ammonia From Blood in Normal and Cirrhotic Patients, New England J. Med. **256**: 941-943, 1957.
2. Dock, W.: Sodium Depletion as a Therapeutic Procedure; the Value of Ion Exchange Resins in Withdrawing Sodium From the Body, Tr. A. Am. Physicians **59**: 282-285, 1946.
3. Flink, E. B., McCollister, R., Prasad, A. S., Melby, J. C., and Doe, R. P.: Evidences for Clinical Magnesium Deficiency, A. M. A. Ann. Int. Med. **47**: 956-966, 1957.
4. Fourman, P.: Depletion of Potassium Induced in Man With an Exchange Resin, Clin. Sc. **13**: 93-110, 1954.
5. Gabuzda, G. J., Phillips, G. B., and Davidson, C. S.: Reversible Toxic Manifestations in Patients With Cirrhosis of the Liver Given Cation-Exchange Resins, New England J. Med. **246**: 124-130, 1952.
6. Greenberg, J. R., Rosenman, L. D., and Lewis, A. E.: Ammonia Content of Stored Blood, J. A. M. A. **165**: 348-349, 1957.
7. Kiley, J. E., Welch, H. F., Pender, J. C., and Welch, C. S.: Removal of Blood Ammonia by Hemodialysis, Proc. Soc. Exper. Biol. & Med. **91**: 489-490, 1956.
8. McDermott, W. V., Jr., and Adams, R. D.: Episodic Stupor Associated With an Eck Fistula in the Human With Particular Reference to the Metabolism of Ammonia, J. Clin. Invest. **33**: 1-9, 1954.
9. Najarian, J. S., and Harper, H. A.: Comparative Effect of Arginine and Monosodium Glutamate on Blood Ammonia, Proc. Soc. Exper. Biol. & Med. **95**: 560-563, 1956.
10. Otto, J. J., Pender, J. C., Cleary, J. H., Sensenig, D. M., and Welch, C. S.: The Use of a Donor Liver in Experimental Animals With Elevated Blood Ammonia, SURGERY **43**: 301-309, 1958.
11. Schechter, D. C., Nealon, T. F., Jr., and Gibbon, J. H., Jr.: Acid-Base Changes in Stored Blood. Submitted for publication.
12. Schechter, D. C., Nealon, T. F., Jr., and Gibbon, J. H., Jr.: The Pretransfusion Removal of Ammonia From Banked-Blood. In press.
13. Schwartz, R., Phillips, G. B., Gabuzda, G. J., Jr., and Davidson, C. S.: Blood Ammonia and Electrolytes in Hepatic Coma, J. Lab. & Clin. Med. **42**: 499-508, 1953.
14. Seligson, D., and Seligson, H.: Microdiffusion Method for Determination of Nitrogen Liberated as Ammonia, J. Lab. & Clin. Med. **38**: 324-330, 1951.
15. Small, S. M., and Maurizi, J. J.: Delirium, Cation-Exchange Resins and Liver Disease, New York J. Med. **55**: 3087-3093, 1955.
16. Spear, P. W., Sass, M., and Cincotti, J. J.: Ammonia Levels in Transfused Blood, J. Lab. & Clin. Med. **48**: 702-707, 1956.
17. Traeger, H. S., Gabuzda, G. J., Ballou, A. N., and Davison, C. S.: Blood Ammonia Concentration in Liver Disease and Liver Coma, Metabolism **3**: 99-109, 1954.
18. Wolff, H. P., Pfeffer, K. H., and Jahrmarker, H.: Mineralstoffwechselstorungen unter Austauscherbehandlung und ihre Vermeidung, Aertzl. Wschr. **10**: 781-788, 1955.

SUPERIOR VENA CAVAL REPLACEMENT

III. Successful Use of Fresh Autogenous Aorta

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THE need for a satisfactory means of superior vena caval replacement or bypass and the unsuitability of most methods which have been attempted have been discussed at length in previous communications.[9, 10] Aorta homografts and synthetic vascular prostheses, materials which have been employed with success both clinically and in the laboratory for arterial replacement, have been found to be unsuitable as venous substitutes.[1-4] Failure also has attended the experimental use for caval replacement of vena caval homografts[6] and of autogenous venous tissue enlarged through the panel technique.[3] Only atriocaval anastomosis, as described by Gerbode and his associates in 1949,[5] and the use of a pedicle tube created from the right atrium and atrial appendage, as reported recently,[10] have been shown to be successful. Despite the success of these two methods, they are limited with respect to the length of proximal superior vena cava which can be replaced.

From the published experience with attempts at venous replacement, it is apparent that success is most likely to be achieved through the utilization of fresh autogenous tissue, particularly endothelized vascular tissue.[1] Prior to the successful use of aortic substitutes, no free autogenous vascular tube of sufficient size was available for vena caval replacement. The availability, at present, of suitable means for replacing resected segments of aorta makes possible the use of free tubes of fresh autogenous aorta for caval replacement. Except for preliminary observations[7, 8] no published experience with the use of fresh autogenous aorta for vena caval replacement or for any other purpose has been encountered. For this reason, it has seemed desirable to report the following experience with the successful experimental use of free tubes of fresh autogenous aorta for superior vena caval replacement.

MATERIAL AND METHODS

Healthy mongrel dogs were used. The weight of the dogs ranged from 12 to 23 Kg. A mixture of oxygen and ether, delivered through an endotracheal tube by means of a mechanical respirator, was employed for anesthesia following induction with intravenous Pentothal. Hypothermia was achieved by immersion of the anesthetized and intubated dog in an ice water bath. The body temperature generally was lowered to approximately 31° C.

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Following removal of the dog from the ice water bath, the left thorax was prepared and draped. The left chest was entered through a fourth or fifth intercostal space incision. The more cephalad portion of the descending thoracic aorta was dissected free from surrounding structures. The intercostal arteries in this area were divided between ligatures. The aorta was occluded with Potts coarctation clamps above and below the sites of proposed transection. The isolated segment of aorta was resected. The resected section of aorta generally measured between 6 and 8 cm. in length. It was placed in a sterile container filled with normal salt solution. The resected aorta was replaced with an alcohol-preserved aortic homograft of approximately the same length. The alcohol-preserved homografts were reconstituted in a normal salt solution containing streptomycin and penicillin for one hour prior to use. The anastomoses were carried out with a continuous over-and-over 5-0 arterial silk suture. In all of the animals, the homografts appeared to function satisfactorily. The left chest was closed in layers. A catheter was left in the left chest for subsequent aspiration.

The dog was turned and the right chest was prepared and draped. A right thoracotomy was performed through a third intercostal space incision. A segment of superior vena cava, ranging from 4 to 6 cm. in length, was resected and replaced with the previously removed segment of fresh autogenous aorta. An over-and-over continuous suture of 5-0 arterial silk was used for both anastomoses. Vena caval occlusion during the resection and anastomosis was maintained by Potts coarctation clamps, the blades of which had been covered with sheaths of filter nylon fabric to prevent caval slippage. The autogenous aorta, at the time of operation, appeared to maintain its lumen and function satisfactorily as a vena caval replacement. Upon completion of the anastomoses, the azygos vein was ligated and divided. No effort was made to cover the caval graft with pleura. The right chest was closed in layers. A catheter was left in the right chest for postwarming aspiration.

The dog's temperature was returned to normal by immersion in a warm water bath. Upon completion of rewarming, both chest catheters were aspirated and withdrawn. Penicillin was given for 4 days following operation.

RESULTS

The operation for superior vena caval replacement with a free tube of fresh autogenous aorta was carried out as described in 33 dogs. The patency of the caval graft was investigated in all animals by cavogram, autopsy, or both from 1 day to 1 year following operation.

Cavograms were made in 14 animals from 2 days to 2 months after operation. The caval graft was found to be patent and functioning satisfactorily in all of them (Fig. 1). Two of the animals studied by cavogram subsequently disappeared from the colony and the cavograms, 8 days and 3 weeks after operating, were the only definitive evidence of graft patency in these animals.

In 31 animals, the suitability of the caval replacement was studied at post-mortem examination. In all of them the caval graft of autogenous aorta

was patent and free of thrombus formation (Fig. 2). Good endothelization of the suture lines was occurring or had occurred in all. The intima retained its normal appearance and there was freedom from contracture and narrowing of the graft. Histologic study of sections from the autotransplants of aorta made at different intervals following operation showed that the cells and structure of the transplant remained viable and healthy in appearance (Fig. 3).

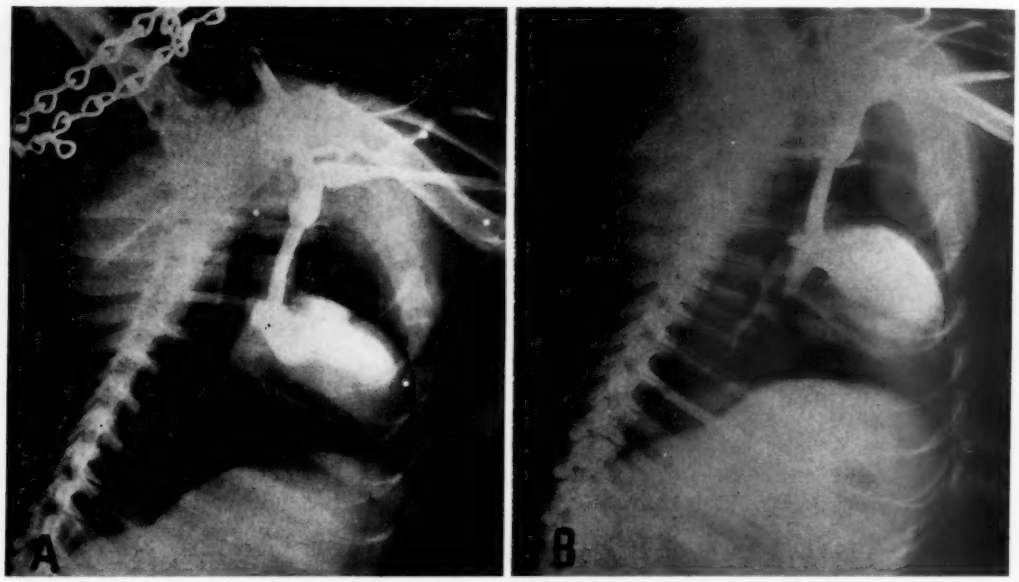

Fig. 1.—Cavograms in 2 animals, 2 (*A*) and 3 (*B*) months after operation, showing patency and satisfactory function of segments of fresh autogenous aorta used for superior vena caval replacement.

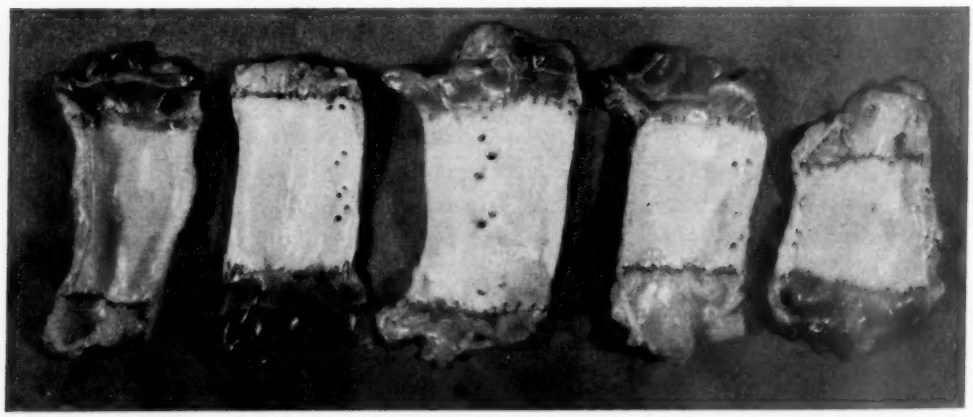

Fig. 2.—Autopsy appearance at sacrifice from 11 to 12 months following operation of segments of autogenous aorta employed for superior vena caval replacement in 5 animals. Graft patency and freedom from thrombosis, narrowing, and degenerative changes are shown.

Fourteen of the animals died from 1 to 14 days after operation. Atelectasis appeared to be the greatest source of difficulty. In 8 of these animals death was due to atelectasis, hemothorax, or infection of the wound and chest. Post-mortem examination was carried out in 5 animals from 4 to 6 weeks following operation. The interval from operation to autopsy in another 7 animals

ranged from 2 to 7 months. Longer term studies were obtained in 5 animals. Two of these animals were sacrificed after an interval of 12 months and 3 after an interval of 11 months. Both the gross and microscopic appearance and the function of the caval grafts were as satisfactory 11 and 12 months after placement as in the early weeks and months following operation.

Although thrombotic occlusion of the aortic homograft used to replace the resected segment of aorta was not encountered in any of the animals in this study, varying degrees of intimal roughening, thrombus formation, and calcium deposition were observed in the majority of them. In a few of the animals, rather sizable thrombi were found attached to the homograft wall or to anastomotic suture lines.

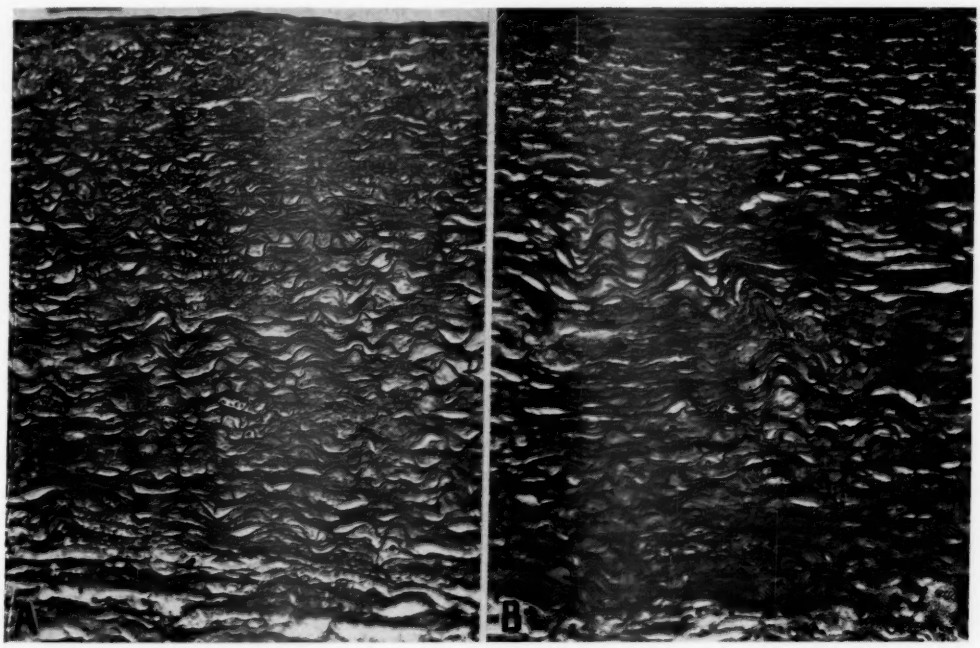

Fig. 3.—Photomicrographs of segments of autogenous aorta used for superior vena caval replacement from 2 animals 11 (*A*) and 12 (*B*) months following operation. The grafts have remained living structures with cells and supporting tissues intact.

The results were quite different in this study of aortic autografts. In this group of 33 animals, the results of caval grafting with fresh autogenous aorta were studied by cavogram only in 2, by both cavogram and autopsy in 12, and by autopsy only in 19. The graft was shown to be patent and functioning satisfactorily in all 33. In all of the 31 animals studied by autopsy, the graft was found to be patent and free of thrombus formation. There was no narrowing of the graft or evidence of calcium deposition. In all, the suture line was endothelized or becoming so. The graft appeared to be tolerated quite well. That the graft had remained a living part of the organism from which it derived its origin was demonstrated by histologic study of sections from numerous grafts at various intervals following operation. The autograft of aorta in the superior vena cava consistently was observed to have a more

normal-appearing intima with greater freedom from thrombus formation and calcium deposition than was encountered in the homograft of aorta in the thoracic aorta of the same animal. It also was of interest that suture line endothelization consistently appeared to proceed at a more rapid rate at the autograft-caval anastomoses than at the homograft-aorta anastomoses.

DISCUSSION

The availability of suitable means for aortic replacement, both by aortic homografts and synthetic vascular prostheses, opens a new avenue of attack on the difficult problem of vena caval obstruction by making it possible to obtain segments of fresh autogenous aorta for use in vena caval replacement or bypass. The consistent success experienced in this study with the use of fresh autogenous aorta for superior vena caval replacement stands in sharp contrast to the rather high degree of failure which has been observed to accompany the use of all other types of free grafts which have been employed clinically and experimentally for vena caval replacement. The manner in which the autograft of aorta was tolerated in the vena cava and its freedom from thrombus formation, calcium deposition, intimal change, and alteration in size and patency were remarkable.

While the use of fresh autogenous aorta for relief of vena caval obstruction, particularly superior vena caval obstruction, may be too formidable to attempt for palliation of obstruction due to malignant processes in most cases, its use in the management of caval obstruction due to benign causes would appear to be worthy of a clinical trial.

SUMMARY

The importance of developing a consistently successful method for relieving vena caval obstruction and the unsuitability of the various types of free grafts described heretofore for use in caval replacement or bypass are discussed. The experimental use of fresh autogenous aorta for superior vena caval replacement in 33 dogs is described.

The fresh autogenous aorta was obtained by resecting a segment of proximal descending thoracic aorta through a left thoracotomy under hypothermia. The resected segment of aorta was replaced with an alcohol-preserved homograft of aorta. A right thoracotomy was used to replace a resected portion of superior vena cava with the fresh segment of autogenous aorta.

All 33 superior vena caval grafts were found to be patent and functioning satisfactorily by cavogram, autopsy, or both from 1 day to 1 year after placement. There was a remarkable freedom from thrombus formation, calcium deposition, and reduction in graft size. Possible clinical applicability of these observations is discussed.

REFERENCES

1. Bryant, M. F., Jr., Lazenby, W. D., and Howard, J. M.: Experimental Replacement of Short Segments of Veins, A. M. A. Arch. Surg. **76**: 289, 1958.
2. DeBakey, M. E.: Quoted by Deterling, R. A., Jr., and Bhonslay, S. B.[3]

3. Deterling, R. A., Jr., and Bhonslay, S. B.: Use of Vessel Grafts and Plastic Prostheses for Relief of Superior Vena Caval Obstruction, SURGERY **38**: 1008, 1955.
4. Gerbode, F.: Discussion of paper by Scannell, J. G., and Shaw, R. S., Surgical Reconstruction of the Superior Vena Cava, J. Thoracic Surg. **28**: 173, 1954.
5. Gerbode, F., Yee, J., and Rundle, F. F.: Experimental Anastomoses of Vessels to the Heart; Possible Application to Superior Vena Caval Obstruction, SURGERY **25**: 556, 1949.
6. Kay, E. B.: Discussion of paper by Scannell, J. G., and Shaw, R. S., J. Thoracic Surg. **28**: 171, 1954.
7. Moore, T. C.: Discussion of paper by Bryant, M. F., Jr., Lazenby, W. D., and Howard, J. M.: Experimental Replacement of Short Segments of Veins, A. M. A. Arch. Surg. **76**: 307, 1958.
8. Moore, T. C., and Riberi, A.: Use of Autogenous Aorta for Superior Vena Caval Replacement; a Preliminary Report, Quart. Bull. Indiana Univ. Med. Center **19**: 59, 1957.
9. Riberi, A., and Moore, T. C.: Superior Vena Caval Replacement. I. Unsuitability of Free Tubes of Autogenous Pericardium, A. M. A. Arch. Surg. **76**: 384, 1958.
10. Riberi, A., and Moore, T. C.: Superior Vena Caval Replacement. II. Successful Use of a Pedicle Tube Created From Right atrium and Appendage, SURGERY **43**: 355, 1958.

PRODUCTION AND RELEASE OF PULMONARY STENOSIS IN DOGS

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WITH the advent of successful cardiopulmonary bypass, there has been a considerable diminution of interest in investigating palliative procedures for patients with interventricular septal defects despite the fact that the mortality from closure of such defects in infants under 2 years remains about 30 per cent.[2] Ventricular septal defect in infancy is a frequent cause of severe and often intractable cardiac failure resulting in a significant mortality during the first year of life. While many of these infants can be tided over with careful medical management, they still face the hazard of progressive pulmonary hypertension related to pulmonary vascular changes which may culminate in progressive and irreversible pulmonary hypertension, reversal of shunt, and death. Therefore, a surgical procedure designed to control the cardiac failure and prevent the development of progressive pulmonary hypertension, if accompanied by a low surgical mortality rate despite the poor condition of the patient at the time of surgery, would seem to be justifiable as a palliative procedure.

Cardiac failure in tetralogy of Fallot is a rarity. Using this as a clinical clue, Muller and Dammann[5] in 1952 described the production of artificial pulmonary stenosis by wedge resection of a segment of the main pulmonary artery in patients with ventricular septal defects and pulmonary hypertension or cardiac failure. Thus by producing a controlled pulmonary stenosis, two adverse factors, pulmonary hypertension and excessive pulmonary blood flow, could be controlled. Since this procedure was intended as a permanent rather than temporary control measure, the method was not designed to allow subsequent restoration of the pulmonary artery to normal.

The present study, therefore, is based upon the demonstrated need for a simple, reversible, palliative surgical procedure which will allow the severely ill infant to survive the critical stage of his illness in order that he may have a definitive closure of his septal defect at a more favorable time in relation to both body size and clinical condition. Over the past 3 years, stenosis of the pulmonary artery has been produced in a number of infants with intractable heart failure due to a large interventricular septal defect by a simple modification of the method of Muller and Dammann. In this procedure the pulmonary

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Abbo-Vac bottles with 15 mg. of heparin supplied by Abbott Laboratories, North Chicago, Ill.

Heparin sodium supplied by Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

artery has simply been constricted by an umbilical tape ligature stenosing the vessel to the desired degree.[1] The present study is concerned with the feasibility of removing the umbilical tape band and the effect on the pulmonary vessel of the umbilical tape band over a period of time.

METHODS

Eleven mongrel dogs weighing from 8 to 20 Kg. were anesthetized with intravenous pentobarbital sodium and insufflated through an endotracheal tube during the operative procedure. The left hemithorax was opened through an anterolateral incision in the fourth or fifth intercostal space; the pericardium was opened widely to expose the base of the pulmonary artery. The pulmonary artery was then dissected free from the aorta and the umbilical tape was passed around it. The ends of the tape were passed through a piece of rubber tubing so that constriction of the pulmonary artery could be carried out slowly and with control (Fig. 1). The artery was then narrowed until a distinct jet

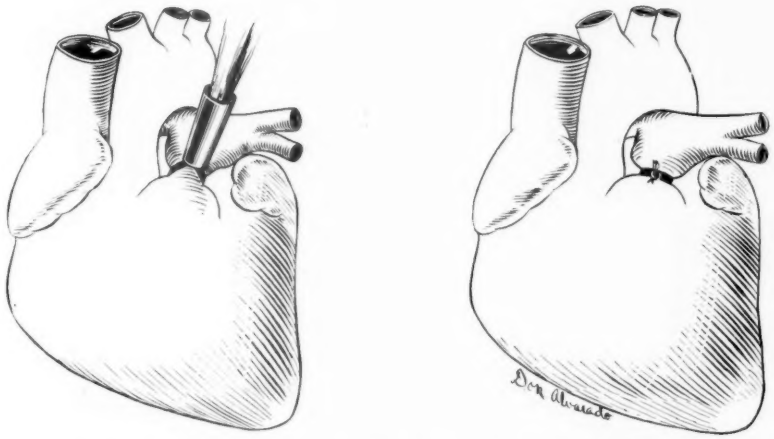

Fig. 1.—Note band is placed immediately distal to pulmonary valve.

of blood striking the vessel wall could be palpated distal to the band. The band was fixed in this position by means of one or two silk sutures through the umbilical tape. An attempt was made to reduce the size of the lumen of the pulmonary artery more than 50 per cent, yet not enough to produce cardiac failure as a result of pulmonary stenosis. In two of these animals an additional mitral stenosis was produced by the Davila-Glover technique.[3] These animals were kept for periods up to 11 months and then reoperated upon using a DeWall-Lillehei type pump-oxygenator to allow opening of the right ventricle. The band was found and isolated only at the site of the knot. The dog was heparinized, the various catheters were introduced, and, with the pump-oxygenator in operation, the right ventricle was opened widely. It was possible then to estimate fairly accurately the size of the lumen of the narrowed portion of the pulmonary artery by introducing a finger or instrument through the pulmonary annulus under direct vision. The band was cut and slipped out and again the size of the lumen was estimated. Dilatation at the stenotic site

was done if necessary, and final estimation of the size was made. The heart was closed, the animal was taken off the pump-oxygenator, and the chest was closed. The animal was kept for another one to two months and finally sacrificed, at which time the amount of residual stenosis, if any, could be measured with accuracy.

RESULTS

Of the 11 animals subjected to the original banding procedure, 8 survived and were reoperated upon after 3 to 11 months (Table I). Two died from intractable heart failure before reoperation, one at one month and one at two months. One died after 5 months from intractable heart failure plus infection. Two of these had the additional creation of mitral stenosis and probably should be excluded from this report. The third dog was the first animal done in this series and the pulmonary stenosis produced was probably too great. It may be interesting to note that this animal had a congenital tricuspid insufficiency corrected 2 months prior to the banding procedure. The 8 surviving animals, although they had a 50 to 75 per cent pulmonary stenosis, had no clinical evidence of physiologic disturbance and remained healthy without special treatment.

TABLE I

DOG NUMBER	PULMONARY ARTERY BANDED	UNBANDING	DEATH
43	Nov. 9, 1956 80%	Jan. 11, 1957	Died in cardiac failure Jan. 11, 1957; tricuspid insufficiency corrected
91	Nov. 5, 1956 60%	July 15, 1957 11 to 20 mm.	Sacrificed Sept. 9, 1957; normal P.A.
199	Nov. 12, 1956 Over 50%	Sept. 30, 1957 Normal size	Died Oct. 1, 1957; hemothorax
1007	Nov. 20, 1956 75%	Sept. 16, 1957 2 to 10 mm. Dilated	Sacrificed Dec. 11, 1957; normal P.A.
1028	Nov. 26, 1956 Over 50%	Sept. 11, 1957 2 to 10 mm. Dilated	Sacrificed Dec. 4, 1957; normal P.A.
1049	Nov. 30, 1956 Over 50%	Sept. 9, 1957 7 to 15 mm.	Sacrificed Dec. 4, 1957; normal P.A.
1046	Dec. 7, 1956 Over 50%	March 11, 1957 Normal size	Died March 11, 1957; pump trial error
1087	Dec. 14, 1956 75%	Oct. 7, 1957 3 to 6 mm. Dilated	Sacrificed Dec. 11, 1957; normal P.A.
10112	Dec. 21, 1956 Over 50%	Aug. 12, 1957 4 to 15 mm.	Died Aug. 13, 1957; pneumothorax
10137	Jan. 7, 1957 Over 50%; mitral valve stenosed		Died May 13, 1957; cardiac failure and infection; band cut through and lying partially in lumen; thrombus extending out right P.A.; marked mitral stenosis with abscess along tape
139	Jan. 15, 1957 Over 50%; mitral valve stenosed	Feb. 21, 1957 Autopsy normal size	Died Feb. 21, 1957; cardiac failure; P.A. normal

At the second operation each dog showed some degree of poststenotic dilatation of the pulmonary artery. When the heart was opened, the size of the stenotic area was found to range from 2 to 11 mm. in diameter. When

the band was removed, 5 dogs showed an immediate restoration in the size of the lumen of the pulmonary artery to approximately the diameter of the pulmonary annulus (15 to 20 mm.). In 3, spontaneous restoration of diameter was to less than 10 mm. and gentle dilatation was necessary to establish a

Fig. 2.

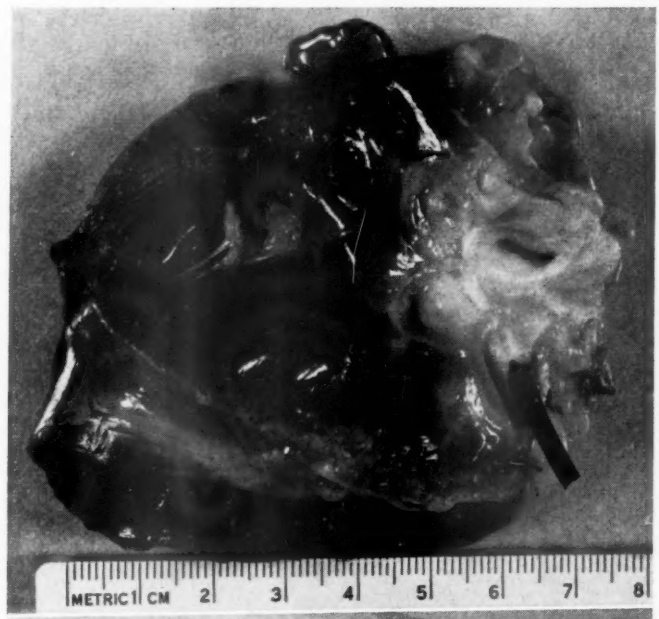

Fig. 3.

Fig. 2.—Arrow points to intimal elevation at banding site. Note absence of stenosis (Dog 1007).

Fig. 3.—Arrow points to elevation of intima at banding site (Dog 1087).

normal-sized lumen. The ease with which the band could be removed was quite remarkable. In every case it was simply a matter of isolating it from surrounding adhesions and scar tissue at the site of the knot. Then as soon as the band was cut, the tape could be slipped out. Of the 8 animals subjected

to the cardiotomy and unbanding procedure with extracorporeal circulation, 5 survived. Three dogs died, one from hemothorax the day after operation, one from blood loss and hemothorax the day after surgery, and one on the operating table shortly after stopping the pump-oxygenator. This last animal was operated upon by error; it had been used as a subject of a trial run of a different pump-oxygenator technique. It was during this run of over one hour that the band was found and removed through the right side of the chest. Death in all 3 of these animals was unrelated to the actual band removal. The 5 surviving animals had uncomplicated postoperative courses and were sacrificed in 2 to 3 months. At autopsy it was often difficult to find the site of previous constriction. Inspection of the interior of the pulmonary artery revealed a small elevation of the intima denoting the previous site of the band (Figs. 2 and 3).

DISCUSSION

Holman and Beck[4] in 1926 produced large interventricular septal defects in dogs and found that if they produced pulmonary stenosis the animal would survive. They, too, used a band around the pulmonary artery to produce the stenosis, but almost invariably their band cut through within a very short period of time. However, they as well as Mont Reid[6] used aluminum bands. Of the 11 dogs in our series, only one tape cut through the pulmonary artery. This was the animal that died at 5 months and in this case there was gross infection involving not only the pulmonary artery and the band around the mitral annulus but also the right and left hemithorax. None of the remaining animals showed any evidence that the band was about to cut through; as a matter of fact, in every other case the band slipped out without difficulty. The difference in results may perhaps be explained on the basis of our using a soft, narrow, cotton umbilical tape placed just distal to the pulmonary valve rather than an aluminum or other band placed more distally.

SUMMARY AND CONCLUSIONS

1. Pulmonary artery stenosis was produced in dogs by banding the vessel with umbilical tape just distal to the valve.

2. The tape bands were removed with ease after a number of months with almost complete restoration in size of the pulmonary artery.

3. The clinical application for this procedure is discussed.

4. From the results of these experiments it can be concluded that the production of pulmonary stenosis with an umbilical tape band is a safe, simple, and reversible procedure in dogs.

REFERENCES

1. Albert, H. M., Fowler, R. L., and Craighead, C. C.: Pulmonary Artery Banding in Infants With Intractable Heart Failure due to Interventricular Septal Defect. In preparation.

2. Cooley, D. A., Belmonte, B. A., DeBakey, M. E., and Latson, J. R.: Temporary Extracorporeal Circulation in the Surgical Treatment of Cardiac and Aortic Disease: Report of 98 cases, Ann. Surg. 145: 898-912, 1957.

3. Davila, J. C., Glover, R. P., Front, R. G., Mansure, F. S., Wood, N. E., Janton, O. H., and Iaia, B. D.: Circumferential Suture of the Mitral Ring, J. Thoracic Surg. **30**: 531-563, 1955.
4. Holman, E., and Beck, C. S.: The Physiological Response of the Circulatory System to Experimental Alterations. III. The Effect of Aortic and Pulmonary Stenosis, J. Clin. Invest. **3**: 283-298, 1926.
5. Muller, W. H., Jr., and Dammann, J. F., Jr.: The Treatment of Certain Congenital Malformations of the Heart by the Creation of Pulmonic Stenosis to Reduce Pulmonary Hypertension and Excessive Pulmonary Blood Flow, Surg., Gynec. & Obst. **95**: 213-219, 1952.
6. Reid, M. R.: Partial Occlusion of the Pulmonary Aorta and Inferior Vena Cava With the Metallic Band. Observations on the Changes in the Vessel Wall and in the Heart, J. Exper. Med. **40**: 289-292, 1924.

MONOPOLAR VENTRICULAR STIMULATION FOR THE CONTROL OF ACUTE SURGICALLY PRODUCED HEART BLOCK

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COMPLETE heart block may occur as the result of inadvertent injury to important conductive elements during repair of congenital cardiac defects, especially those of the interventricular septum. The difficulty in management and high mortality rate associated with this condition have been noted many times in the literature.[2, 3, 5] The need for a therapeutic approach in addition to drugs has become evident because of the failure of the latter to provide an effective control.

As an aid in the treatment of heart block acquired from chronic heart disease, Zoll and his co-workers[11] have described the effectiveness of an externally applied artificial pacemaker in tiding patients over periods which would otherwise have been fatal. This system, primarily designed to obviate a thoracotomy, has untoward effects which would be undesirable during the postoperative period. These include chest pain, muscle twitching, removal of sterile dressings for proper electrode placement, and ulcers beneath the electrodes.

Weirich and associates[10] reported experimental and clinical use of direct ventricular pacemaking in surgical heart block and demonstrated a significant reduction in mortality with this technique. The following studies also demonstrate the effectiveness of this method and support its use clinically.

METHODS

Eleven healthy mongrel dogs weighing 8 to 12 Kg. were used. After premedication with morphine and atropine the dogs were anesthetized with ether. Intubation was then carried out and an ether-air mixture was administered by means of a mechanical respirator. Thoracotomy was performed through the fifth right intercostal space. Complete heart block was created by section of the bundle of His through a right atriotomy during temporary caval occlusion.[7] The myocardial electrode consisted of No. 28 stainless steel wire insulated with a thin layer of Teflon.* About 3 mm. of the end of the wire was denuded to insure good contact, implanted into the right or left ventricular wall, and held in place with a single suture (Fig. 1). The wire was led out through a needle wound and the chest was closed. When the dogs were fully awake they were comfortably restrained in a specially constructed metal frame and long-term cardiac pacemaking was begun. The artificial pacemaker

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consisted of a stimulator which produced monophasic, square wave electric impulses with a duration of three milliseconds. Two controls allowed variations in frequency up to 200 stimuli per minute and amplitudes up to 150 volts. Since a constant current stimulus was desired a resistance (47 K.) which was large in comparison with that of the dog (480 to 850 ohms) was placed in series with the positive electrode. This modification allowed a range of approximately 0 to 8 milliamperes. The negative pole of the stimulator was attached to the myocardial electrode (cathode) and the positive pole to a No. 22 hypodermic needle (anode) piercing the skin at any convenient site.

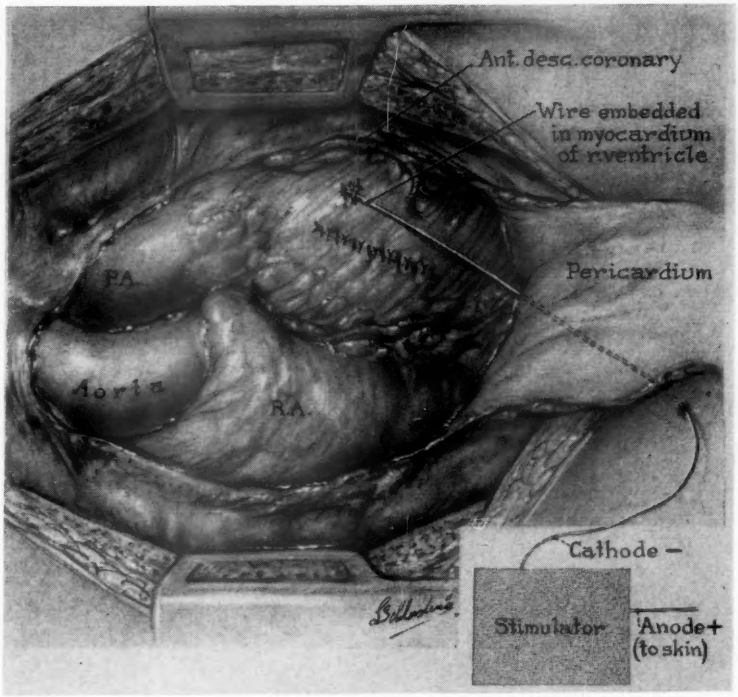

Fig. 1.—Artist's view of the technique used for the control of acute surgically produced heart block.

Femoral artery pressures were obtained daily through an indwelling catheter and registered through a Statham strain gauge along with the electrocardiogram (lead II) on a Sanborn recorder. The current and voltage thresholds (during diastole) necessary for complete control of the cardiac cycle were obtained daily by means of an oscilloscope. Pacemaking was carried out at one milliampere above threshold to insure a safe margin. At the end of the period of stimulation, 5 of the 11 dogs were sacrificed. The myocardial electrode was pulled out of the remaining 6 dogs and these were allowed a further survival of 2 weeks. Histologic sections were taken at the site of implantation in all animals. A similar method and pacemaker has been used on 4 patients who developed complete heart block during intracardiac surgery.

RESULTS

Repetitive ventricular stimulation was carried out for periods of 2 to 10 days in 11 dogs in which complete heart block had been established previously.

The idioventricular rates ranged from 7 to 74 per minute and pacemaking was carried out at rates of 102 to 120 per minute (Table I). The thresholds (during diastole) ranged from 1.3 to 2.8 milliamperes and 0.9 to 1.7 volts. These values remained essentially the same throughout the period of stimulation. The electrical resistance of this circuit, as calculated from Ohm's law, ranged from 480 to 850 ohms. Changing the position of the positive electrode on the skin had no effect upon threshold values. When pacemaking was begun at a

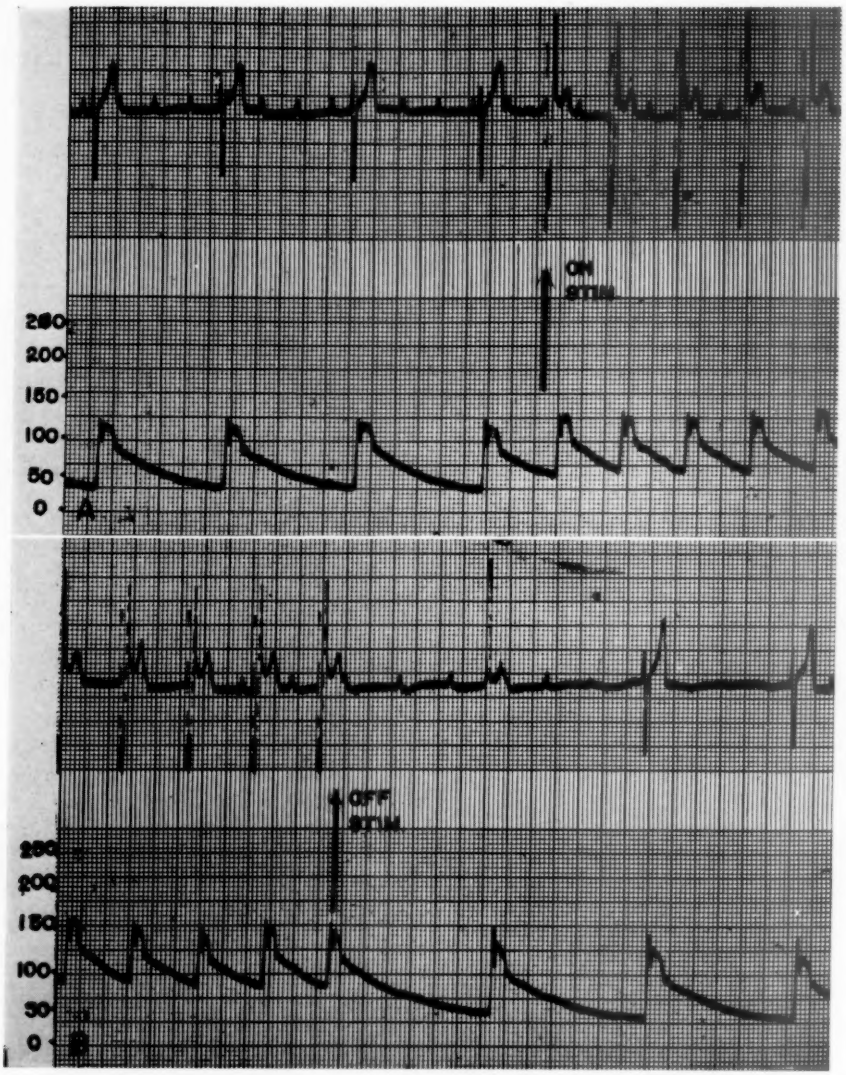

Fig. 2.—Dog. 1. Electrocardiographic (lead II) and blood pressure tracings taken at (*A*) the onset of stimulation and (*B*) cessation of stimulation after 10 days.

rate faster than the idioventricular one, the ventricular cycle was readily brought under control, and there were no spontaneous ventricular discharges. The driven electrocardiogram appeared as uniform QRS complexes preceded by a stimulus artifact, and the P waves continued at their previous rate. During pacemaking the systolic pressure remained essentially as before with the

diastolic pressure becoming elevated. When stimulation was finally stopped, as well as during brief daily recordings without stimulation, the heart rate, arterial pressure, and electrocardiographic configuration promptly returned to original values (Fig. 2). There were a few instances, however, in which up to 14 seconds were required before the ventricles regained their original rates. In one dog the production of heart block resulted in an idioventricular rate of 7 per minute and pacemaking was begun immediately. As shown by the long

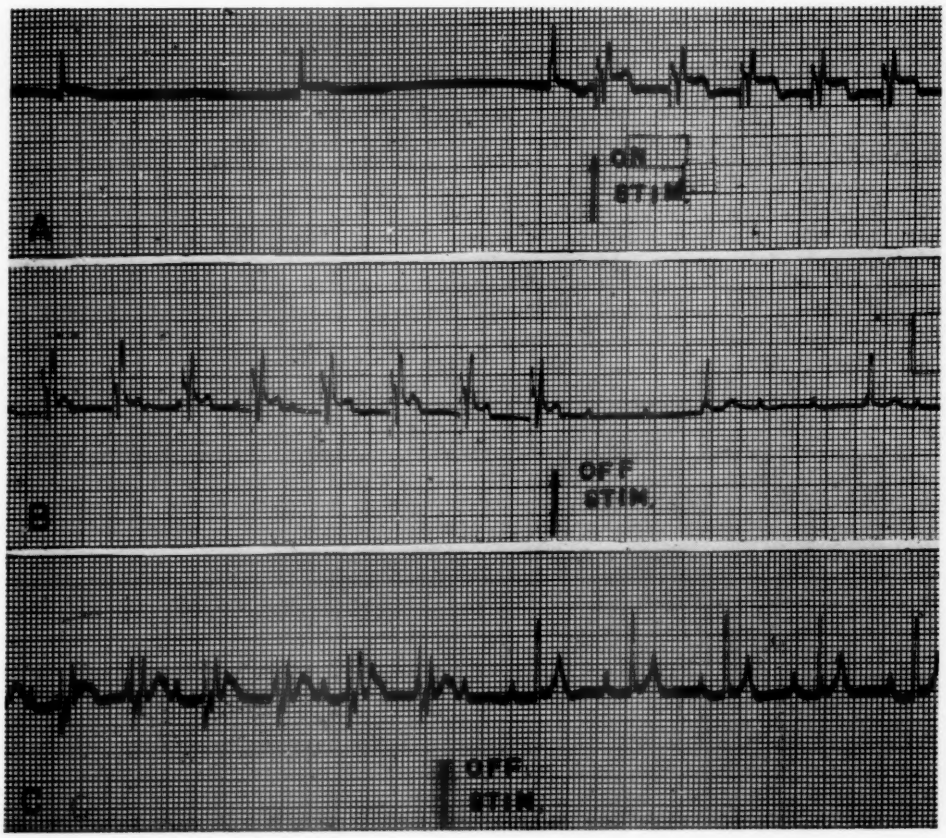

Fig. 3.—Dog 3. Electrocardiographic (lead II) tracings taken at (*A*) the onset of stimulation and (*B*) on the seventh day of stimulation. Note the persistence of a complete heart block, (*C*) reversion to a sinus rhythm with cessation of stimulation after 8 days. This reversion was permanent.

TABLE I. THE DURATION, RATE, AND THRESHOLD OF STIMULATION

DOG NUMBER	IDIOVENTRICULAR RATE (BEATS/MIN.)	STIMULATION RATE (BEATS/MIN.)	DURATION OF STIMULATION (DAYS)	CURRENT THRESHOLD (MA.)	VOLTAGE THRESHOLD (VOLTS)
1	60	114	10	1.3	0.90
2	54	119	6	1.3	0.98
3	46	111	8	1.4	1.10
4	53	120	9	1.5	1.13
5	51	117	7	2.0	1.70
6	60	120	5	1.5	1.04
7	7	102	2	2.0	1.60
8	36	120	5	1.8	0.94
9	74	117	4	2.8	1.35
10	60	120	7	2.0	1.50
11	60	120	6	1.5	1.13

asystole in Fig. 3, this animal would have been unable to survive without the pacemaker. Unfortunately, accidental exsanguination occurred due to a poorly fixed indwelling arterial catheter after 48 hours of pacemaking. One of the 11 dogs reverted to a sinus rhythm on the eighth day of stimulation (Fig. 4).

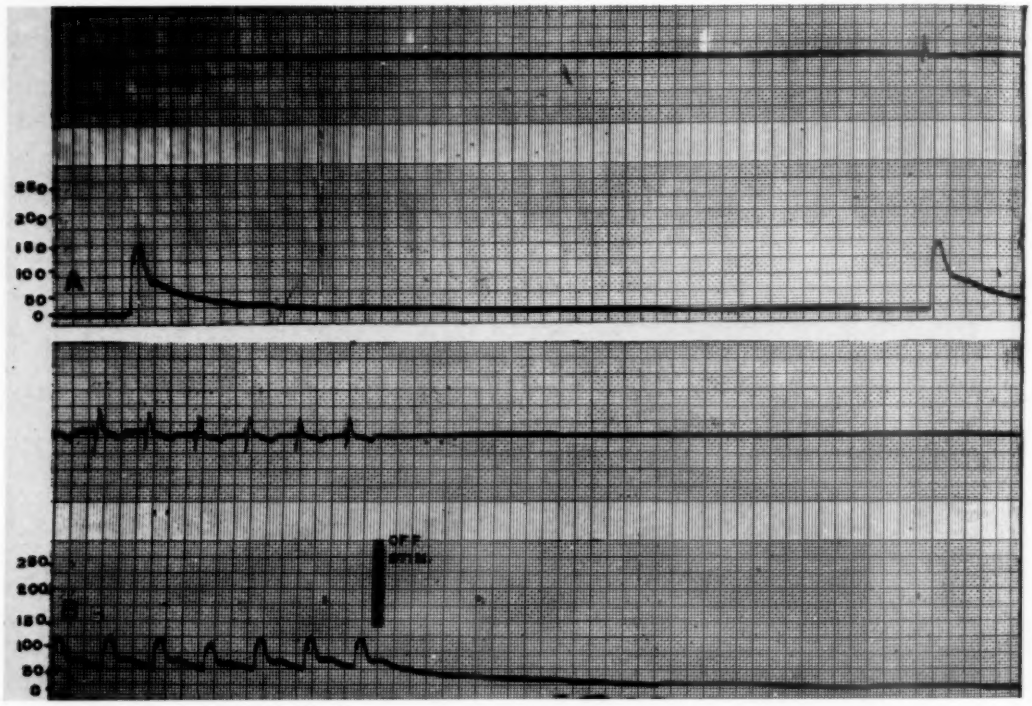

Fig. 4.—Dog 7. Electrocardiographic (lead II) and blood pressure tracings taken (*A*) after the surgical production of heart block. Note the extreme bradycardia and low amplitude of the QRS complex, (*B*) cessation of stimulation after 48 hours. Note the failure of a spontaneous idioventricular beat.

There were no untoward effects noted as the result of removal of the myocardial electrode in the 6 dogs allowed a further survival period. Histologic examination at the site of wire implantation revealed minimal tissue damage. Neither the experimental animals nor the patients reported below appeared to experience any discomfort as a result of the procedure.

CASE REPORTS

CASE I.—D. K. (H.L.H. No. B-31688), an 11-month-old girl weighing 4 Kg., was admitted to The Johns Hopkins Hospital on Nov. 8, 1956, for evaluation of a congenital cardiac defect. Cardiac catheterization confirmed the presence of a patent ductus and gave clear-cut evidence of an interventricular septal defect. Pressure in the pulmonary artery was 73/36 mm. Hg. There was a small left-to-right shunt at the defect and also at the level of the ductus. Just prior to operation bradycardia was noted. At operation the ductus was doubly ligated. During cardiopulmonary bypass with a Gaertner-Kay heart-lung machine,[4] a high interventricular septal defect was repaired by direct suture through a right ventriculotomy. Twelve milliliters of a 2 per cent potassium citrate solution was used to produce cardiac asystole, and, when coronary flow was reopened, the heart's action returned slowly showing a complete heart block with severe bradycardia. Accordingly, a

Teflon-coated wire was implanted on the right ventricle and was brought out through a needle inserted in the epigastrium, and pacemaking was begun before the chest was closed. The threshold to stimulation was 1.6 milliamperes. Adequate blood pressures were maintained during stimulation. In the first few hours after surgery the patient was unable to take over during several attempts to stop pacemaking. The patient was alert and did well for the first 10 postoperative hours. However, after this, there was a rapid deterioration and the patient expired despite the concomitant use of drugs and final open manual systole.

CASE 2.—P. K. D. (J.H.H. No. 763159), a 2-year-old girl weighing 10.5 Kg., was admitted to The Johns Hopkins Hospital on Feb. 10, 1957, for treatment of a congenital cardiac defect. Cardiac catheterization confirmed the diagnosis of an interventricular septal defect and revealed a pulmonary artery pressure of 93/38 mm. Hg. The severe pulmonary hypertension was felt to make surgery urgently indicated. At operation the heart was arrested with 7 c.c. of a 2 per cent potassium citrate solution during cardiopulmonary bypass. Complete closure of an interventricular defect of the membranous septum was performed through a right ventriculotomy. With return of the heart's activity a complete heart block was evident and a wire was implanted for stimulation. The heart block was treated adequately with Isuprel for 10 hours following surgery when sudden cardiac arrest occurred. The pacemaker was turned on, bringing the cardiac cycle into immediate control, and the patient remained alert and conscious. About 15 minutes later the pacemaker was discontinued and the patient was able to maintain what was thought at the time to be an adequate idioventricular rate until 24 hours after surgery when a second sudden cardiac arrest occurred. The pacemaker again brought the cardiac cycle under immediate control. After 20 hours of pacemaking, a gradual deterioration occurred despite the concomitant use of drugs and the patient expired, becoming terminally unresponsive to stimulation.

CASE 3.—L. G., an 8-year-old boy was treated during a visit to the Royal Prince Alfred Hospital, Sydney, Australia. He was moderately incapacitated with a ventricular septal defect which was repaired during cardiopulmonary bypass and elective asystole with potassium citrate. Complete heart block was evident when the heartbeat was restored and the ventricular rate was about 60 per minute. A wire electrode was implanted and stimulation was begun on the operating table at a rate of 90, with a resulting increase in blood pressure. During the day, increasing the rate of stimulation to 110 to 120 per minute was associated with a rise in directly measured arterial pressure, and stimulation was continued at this rate for the next 5 days. On several occasions during this period, stimulation was stopped for brief periods to determine the idioventricular rate and on one occasion when the patient unknowingly disconnected the indifferent electrode on the leg. On each occasion the ventricular rate fell to around 50 and he became unconscious, once having a brief convulsion.

On the fifth postoperative day a supraventricular tachycardia appeared which the ventricles followed at a rate around 150. Over the next 3 days this rhythm alternated with a complete block and sinus rhythm. A week after operation sinus rhythm persisted and the electrode was removed several days later.

CASE 4.—P. W. (J.H.H. No. 687454), a 7-year-old girl, was admitted to the Johns Hopkins Hospital on Nov. 11, 1957, for repair of a ventricular septal defect. This was done during cardiopulmonary bypass and 10 minutes of elective asystole. Cardiac contractions returned with a complete atrioventricular dissociation and a ventricular rate of 70 to 80. A wire electrode was implanted in the right ventricle. Although the ventricular rate was not strikingly slow, the systolic blood pressure increased from 70 to 90 when the ventricles were driven at a rate of 105 per minute. Pacemaking was continued for 6 days. At intervals during this time the strength and duration of the stimulus had to be increased. This may have been due to poor electrical connections. On the sixth day there was no change in blood pressure when the pacemaker was stopped and it was permanently discontinued. The wire was pulled out one week later. While in the hospital, ventricular rates ranged

from 42 at night to 60 per minute during the day without drugs and with no evidence of detriment. The patient was continuing to improve when heard from at 3 months but died suddenly 5 months after operation, presumably from asystole.

DISCUSSION

Important structures of the cardiac conduction system are known to be intimately related to interventricular septal defects. Reemtsma and Copenhaver[6] have indicated that the atrioventricular bundle courses along the posteroinferior margin of the ventricular defect in a subendocardial position. During repair of these defects, damage to important conductive elements would seem unavoidable in some instances. The most plausible explanation for heart block produced in this manner is direct injury. Other factors such as hypothermia, hyperkalemia, anesthesia, overdigitalization, or anoxia might be incriminated in the initial production of heart block, the block thus being continued in the poorly functioning slow heart. The importance of these and other nonanatomic factors is demonstrated clinically in experience at this hospital in which emphasis on cessation of digitalis 2 to 3 days before operation, light anesthesia, maintenance of body temperature, and continued care in the placing of sutures in the critical posterior rim of defects of the membranous septum has been associated with a decrease in incidence of block from 9 in the first 23 (40 per cent) patients with ventricular septal defects to 2 in the last 29 (7 per cent).

The surgical production of an acute complete heart block may severely diminish the cardiac output and mean arterial pressure. The effectiveness of repetitive ventricular stimulation after the surgical induction of acute heart block has been shown by Starzl and his co-workers,[8, 9] who demonstrated that stimulation of the ventricles at preblock rates restores the cardiac output and systemic pressure to preblock levels and is independent of the site on the ventricle at which stimulation is given.

When a block is inadvertently produced during repair of a cardiac defect, cardiac function is most severely stressed during the first 48 to 72 hours. This indicates that pacemaking, with the addition of drugs as needed, should be started early in the critical postoperative period and certainly before any obvious signs of failure or impending breakdown of the idioventricular pacemaker are seen. Once maintained through this period, cardiac function gradually improves to allow survival despite a permanent heart block. This condition is seemingly less dangerous in young patients than in the elderly but remains a hazard as shown by Case 4. In 2 patients treated here before stimulation was in use, the block spontaneously disappeared a few days after operation in one and several months later in the other. Such reversion to sinus rhythm was seen in one of the experimental animals. This phenomenon is most readily explained in terms of resolution of edema and inflammation and improvement of cardiac function.

The position of either electrode is not critical and a convenient site on the right ventricle and on the skin was selected. The polarity, however, is critical since the threshold during diastole is lower with cathodal rather than

anodal monopolar stimulation.[1] The duration of the stimulus is important since inspection of strength-duration curves for the ventricle reveals that shocks less than 3 milliseconds require a much higher strength of current.[1] The intensity of heat produced by stimuli of short duration might lead to tissue damage. The fact that, in the dog, threshold levels remained constant daily was taken as evidence that no tissue damage occurred as a result of the strength of electric current used. This was confirmed by microscopic study of the site of implantation of the cardiac electrode. Changes in threshold were not as carefully measured in Case 4 and it was believed variations were influenced by surface electrode contacts.

Weirich and his co-workers[10] have reported the experimental and clinical use of direct ventricular pacemaking in controlling heart block due to intracardiac surgery. It is encouraging that the mortality rate was remarkably reduced by the successful use of this technique in 18 patients.

There are undoubtedly some patients with surgical atrioventricular block in whom pacemaking cannot prevent deterioration of cardiac function, since heart block is an important sign of cardiac disease. Such was believed to be the situation in Case 1. Similarly, pacemaking must be started before irreversible changes have occurred. It is thus important in most instances to begin pacemaking in the operating room. The level of arterial pressure has been a helpful criterion of the optimal rate. We believe Case 2 would probably have survived if early continuous stimulation had been used.

SUMMARY

The effectiveness of ventricular stimulation in the treatment of surgical heart block was demonstrated experimentally in 11 dogs. A wire electrode was implanted in the ventricle after the surgical division of the conducting tissue. By means of repetitive electrical discharges through this electrode, these animals were pacemade continuously for periods up to 10 days at frequencies well above the blocked rates. At the end of this period the electrode was removed without untoward effects. The amount of current necessary was 1.3 to 2.8 milliamperes at 0.9 to 1.7 volts.

Use of this technique in 4 patients has been described and the beginning of stimulation during or immediately after operation emphasized.

We are grateful for the technical assistance of Julius Mayo.

REFERENCES

1. Brooks, C. M., Hoffman, B. F., Suckling, E. E., and Orias, O.: Excitability of the Heart, New York and London, 1955, Grune & Stratton, Inc., pp. 67-70, 86-90.
2. Cooley, J. C., Kirklin, J. W., and Harshbarger, H. G.: The Surgical Treatment of Persistent Common Atrioventricular Canal, SURGERY **41**: 147-152, 1957.
3. DuShane, J. W., Kirklin, J. W., Patrick, R. T., Donald, D. E., Terry, H. R., Jr., Burchell, H. B., and Wood, E. H.: Ventricular Septal Defects With Pulmonary Hypertension; Surgical Treatment by Means of a Mechanical Pump-Oxygenator, J. A. M. A. **160**: 950-953, 1956.
4. Kay, J. H., and Gaertner, R. A.: A Simplified Pump-Oxygenator With Flow Equal to Normal Cardiac Output, S. Forum, **7**: 267-271, 1956.

5. Lam, C. R., Gahagan, T., Sergeant, C., and Green, E.: Clinical Experiences With Induced Cardiac Arrest During Intracardiac Surgical Procedures, Ann. Surg. **146**: 439-449, 1957.
6. Reemtsma, K., and Copenhaver, W. M.: Anatomic Studies of the Cardiac Conduction System in Congenital Malformations of the Heart, Circulation **17**: 271-276, 1958.
7. Starzl, T. E., and Gaertner, R. A.: Chronic Heart Block in Dogs. A Method for Producing Experimental Heart Failure, Circulation **12**: 259-270, 1955.
8. Starzl, T. E., Gaertner, R. A., and Baker, R. R.: Acute Complete Heart Block in Dogs, Circulation **12**: 82-89, 1955.
9. Starzl, T. E., Gaertner, R. A., and Webb, R. C., Jr.: The Effects of Repetitive Electric Cardiac Stimulation in Dogs With Normal Hearts, Complete Heart Block, and Experimental Cardiac Arrest, Circulation **11**: 952-962, 1955.
10. Weirich, W. L., Gott, V. L., and Lillehei, C. W.: The Treatment of Complete Heart Block by the Combined Use of a Myocardial Electrode and an Artificial Pacemaker, S. Forum, **8**: 360-363, 1957.
11. Zoll, P. M., Linenthal, A. J., Norman, L. R., Paul, M. H., and Gibson, W.: External Electric Stimulation of the Heart in Cardiac Arrest, A. M. A. Arch. Int. Med. **96**: 639-653, 1955.

SECOND SHUNTING OPERATIONS FOR PULMONARY STENOSIS WITH CYANOSIS FOLLOWING FAILURE OF ORIGINAL SYSTEMIC-PULMONARY ANASTOMOSES

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IN THE 13 years' experience with systemic-pulmonary shunts for pulmonary stenosis at The Johns Hopkins Hospital, a number of patients have required a second operation to further augment pulmonary blood flow. A study of the conditions which necessitated reoperation in these cases, analysis of the surgical techniques employed, and evaluation of the results achieved following the second anastomosis constitute the purpose of this paper.

Between November, 1944, and November, 1957, 1,500 patients with pulmonary stenosis and cyanosis were treated by creation of a systemic-pulmonary anastomosis. A detailed follow-up of the first 1,000 cases was reported by Taussig in 1953.[3] A large majority of those who survived the hospital period were immediately benefited; in many cases the favorable results have been maintained. In the group as a whole, however, 109 patients have been reoperated upon because the initial procedure became inadequate.

To facilitate analysis of the reoperated cases and the original group, the patients have been divided into 4 age groups: less than 2 years, 2 to 5 years, 5 to 12 years, and over 12 years. This is an arbitrary grouping, but it takes cognizance of the fact that the small infant and the teenager constitute different technical problems in arterial anastomosis. This division also separates the clinically ideal age group for the subclavian-pulmonary anastomosis, 5 to 12 years, and the 2 to 5 year age group in which the best shunting procedure has not been established. In the latter group the recommendations for type of operation remain highly subjective and warmly debated. As shown in Table I there were 34 patients (31 per cent) in Group 1, 44 patients (40 per cent) in Group 2, 18 patients (16 per cent) in Group 3, and 13 patients (12 per cent) in Group 4.

There were 3 different clinical courses which ultimately resulted in a need for reoperation. Some patients had no continuous murmur from the early postoperative period, indicating *immediate thrombosis* of the anastomosis. These patients were usually unchanged by operation and often needed early second procedures. Other patients left the hospital with an open anastomosis and were definitely benefited by operation, but in the ensuing months or years the continuous murmur disappeared and was associated with the return of cyanosis

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and symptoms; these are assumed to have had *late thrombosis.* A larger third group continued to have anastomotic murmurs, but because of a relative increase in body size from normal growth their shunts became inadequate and polycythemia and dyspnea on exertion slowly returned. The last patients are considered to have *outgrown* their formerly adequate shunts. These 3 clinical courses were found in all age groups, but specific differences are noted in the group analyses.

TABLE I

GROUP	AGE (YEARS)	INITIAL OPERATION		SECOND OPERATION		REASON FOR SECOND OPERATION†		MORTALITY (PER CENT)
		NUMBER	PER CENT	NUMBER	PER CENT	THROMBOSED ANASTOMOSIS	GROWTH OF PATIENT	
1	0-2	266	18	34*	31	19	15	20
2	2-5	514	34	44	40	7	37	5
3	5-12	478	32	18	16	5	13	6
4	12	242	16	13	12	6	7	0
Total		1,500		109		37	72	9

*Four had 3 shunting procedures.
†Potts anastomosis in 52 per cent.

TABLE II

	TYPE OF FIRST OPERATION		INTERVAL BETWEEN OPERATIONS		TYPE OF SECOND OPERATION		
	END-TO-SIDE SUBCLAVIAN-PULMONARY	END-TO-END SUBCLAVIAN-PULMONARY	RANGE IN YEARS	AVERAGE IN YEARS	END-TO-SIDE SUBCLAVIAN-PULMONARY	END-TO-END SUBCLAVIAN-PULMONARY	POTTS
Group 1 (0 to 2 years)							
Thrombosis	14	5	7 days-9 years	3	15	3	16
Outgrown	14	1	4-10	6			
Group 2 (2 to 5 years)							
Thrombosis	6	1	1 month-8 years	4	11	4	28*
Outgrown	37	0	2-11	6			
Group 3 (5 to 12 years)							
Thrombosis	4	1	2-92	5	6	1	11
Outgrown	13	0	5-12	8			
Group 4 (over 12 years)							
Thrombosis	5	1	2 months-9 years	3	5	6	2
Outgrown	5	1	2-8½	5			
Too large Potts	1						
Summary					37	14	57†
Thrombosis	29	8					
Outgrown	69	2					
	98	10					
Too large Potts	1						

*One second operation in Group 2 was an infundibular resection.
†Nine required homografts between aorta and pulmonary artery—all in patients with right aortic arches.

In the infant age group there were 34 patients of whom 19 (56 per cent) were reoperated upon because of thrombosis of the anastomosis (Table I). Sixty per cent of these thromboses occurred immediately or during the hospital stay while the others were late thromboses. When the indication for second operation was thrombosis, the average interval was 3 years with a range of 7 days to 9 years. This wide range reflects the fact that the immediate thromboses were often reoperated upon while in the hospital, but the late ones were observed much longer. One-third of the patients with thrombosis had had end-to-end anastomoses (Table II). Since this anastomosis is not used electively, but only if the vessels are too small or too short for an end-to-side anastomosis, the high incidence of the end-to-end type (nearly one-fifth) indicates the frequency of major technical problems in the infant age group. This unfavorable situation is reflected in the high thrombosis rate.

The 15 patients in the infant age group who outgrew their shunts had an average interval between operations of 6 years with a range of 4 to 10 years (Table II). This longer interval underlines the definite improvement achieved even though further augmentation of pulmonary flow became necessary for the increased body growth.

The second operations employed in this infant age group were equally divided between the Potts type and a subclavian-pulmonary anastomosis on the opposite side. The operative mortality was 20 per cent. Four patients in this group required 3 shunting procedures; 3 died during or shortly after the third operation. The fourth patient had an end-to-side anastomosis at 13 months which thrombosed in the hospital, then an end-to-side anastomosis on the other side at 14 months which also thrombosed in the hospital, and finally a Potts anastomosis at 23 months which has remained open with satisfactory clinical improvement maintained for 5½ years.

In the 2 to 5 year age group there were 44 patients but only 7 (16 per cent) required reoperation because of thrombosis. Six of the 7 developed thrombosis during the first postoperative week. The average interval between operations when thrombosis occurred was 4 years. It is prognostically significant that only one of 38 patients who were discharged with continuous murmurs had the murmur disappear later. If thrombosis did not occur immediately, it was very unlikely in this age group. The interval between operations for those who outgrew their shunts was 6 years, somewhat longer than for those with thrombosis.

At the initial operation all the patients in this group had subclavian-pulmonary end-to-side anastomoses with a single exception—one patient had an end-to-end anastomosis which thrombosed in the hospital. Three-fifths of the second operations were of the Potts type, in several cases employing arterial grafts. The operative mortality was 5 per cent. A Potts anastomosis was used predominantly because the first operation was usually on the right side, and with the second operation on the left or arch side the subclavian vessel in most cases did not make a favorable angle from the aorta for a good pulmonary anastomosis.

There were 18 patients in Age Group 3, ages 5 to 12 years. Five (28 per cent) were reoperated upon because of thrombosis; 3 of these were late throm-

boses and 2 occurred during the hospital stay. The average interval between operations was 5 years in the case of thrombosis and 8 years when the shunt was outgrown. The interval between operations for thrombosis is longer than in the former groups and reflects the higher incidence of late thrombosis. None of these patients with late thrombosis had other illnesses at the time their murmurs disappeared. Subacute bacterial endocarditis cannot be implicated; the etiology is obscure. Seventeen of the 18 patients in Age Group 3 had subclavian-pulmonary end-to-side anastomoses originally; one had an end-to-end shunt which thrombosed. Eleven or two-thirds of the second operations were of the Potts type. Ten of these 11 patients had original shunts on the side opposite the aortic arch. Because of a right arch 4 required arterial grafts for the aortic-pulmonary shunt on that side. The operative mortality was 6 per cent.

Thirteen patients requiring reoperation were over 12 years of age at the time of this first operation and constitute Age Group 4. Six had thrombosis of the anastomosis; 3 occurred in the hospital and 3 were late thromboses. The average time interval between operations was 3 years. Six patients had patent anastomoses when the second procedure was performed. The average time interval between operations in these 6 patients was 5 years. These patients apparently required a larger shunt than a single subclavian vessel could carry or else there was progressive narrowing of the primary anastomosis. There is no evidence that an anastomosis will decrease in size 5 to 6 years after operation, so the best explanation is that these patients required more flow than the single shunt could provide. One patient was reoperated upon to close a primary Potts anastomosis which was too large and associated with intractable failure. It is the only case in the whole reoperated series where the indication for operation was too much flow rather than too little.[2] Ten of the original operations were end-to-side procedures, 5 thrombosed; two were end-to-end anastomoses, one thrombosed. Six of the second operations were end-to-end subclavian-pulmonary anastomoses, 4 end-to-side, 2 Potts, and 1 pulmonary valvulotomy. There were no operative or late mortalities.

TABLE III. CRITERIA USED FOR FOLLOW-UP EVALUATION AFTER SECOND OPERATION

Unsatisfactory:		Persistently high or rising hematocrit. Severe limitation of activity. Congestive failure or enlarging heart with dyspnea.
8	6 had	signs of too great shunt (Potts 1).
	2 had	signs of too small shunt (Potts 2).
Satisfactory:		Relatively stable course. Moderate polycythemia but not progressive. Minor limitation of activity. Moderate cardiac enlargement controlled with digitalis.
23	10 had	signs of too great shunt (Potts 5).
	13 had	signs of too small shunt (Potts 3).
Well:		No cardiac symptomatology except on severe exertion. No exercise limitation. Normal hematocrit. Treated as normal children.
52	39	shunt balanced with stenosis, hematocrit normal and heart size normal (Potts 26).
	4 had	minor evidence of too large shunt (Potts 3).
	9 had	minor evidence of too small shunt (Potts 4).

The clinical evaluation of the postoperative courses in this group of reoperated patients is necessarily highly subjective. It would be fallacious to tabulate graded signs and symptoms and fluoroscopic interpretations when no detailed follow-up protocol was used by all examiners and when different physicians saw the patients on their return visits to the Cardiac Clinic. Nevertheless the patients reoperated upon have been placed in 3 categories based upon the criteria outlined in Table III. This division represents the present clinical status of the 83 patients who have been followed more than 3 months since their second operation. Table IV shows the distribution of these patients in the various age groups and gives the follow-up time periods since the second operation.

TABLE IV

GROUP (NUMBER OF PATIENTS)	DEAD		FOLLOW-UP SINCE SECOND OPERATION		PRESENT STATUS		
	OPERATION	LATE	RANGE	AVERAGE	UNSATISFACTORY	SATISFACTORY	WELL
1 (34)	7	1	4 months-9 years	3 years	2	5	14
2 (44)	2	0	3 months-8 years	2½ years	2	6	27
3 (18)	1	1*	4 months-7 years	2½ years	2	5	7
4 (13)	0	0	3 months-7 years	2½ years	2	7	4
Total (109)	10	2			8	23	52

Number not evaluated because follow-up less than 3 months = 12.
Lost to follow-up = 2.
*Attempted open heart repair.

DISCUSSION

Of particular pertinence is how the age distribution in the entire series of 1,500 compares with the distribution in the group reoperated upon (Table I). Eighteen per cent of the entire series fall into Age Group 1, whereas 32 per cent of the patients reoperated upon fall into this group. Fifteen per cent of all children less than 2 years old who presented themselves for operation required reoperation. The majority of these infants had thrombosis of the anastomoses, most of them in the immediate postoperative period. This fact further emphasizes the technical difficulties associated with anastomoses between very small vessels and underlines the desirability of waiting for additional growth if at all possible. However, in the majority of these patients the shunting procedure could not be postponed because of the severe stenosis and grave cyanosis. To illustrate the critical status of these infants, each was given a preoperative "risk rating" based upon severity of spells, degree of cyanosis, and general condition. Thus each received a good, fair, or poor "risk rating" before surgery. In this infant age Group, one-half of the patients were considered poor risks; only 3 were good risks. This is to be compared with the children in the most favorable Age Group 3 (5 to 12 years) in which 80 per cent were good risks and none was considered a poor risk.

In the total series 34 per cent fall into Age Group 2 (2 to 5 years); 40 per cent of the patients reoperated upon fall into this group. Nine per cent

of the patients in this age group required a second anastomosis, but, whereas thrombosis was the indication in most of the infants in Age Group 1, 85 per cent of these children required reoperation because they had grown too big for their shunts. At least these children had a period of fairly normal growth, a fact of considerable satisfaction to the parents as well as to the physician. This is a more heartening picture than in Age Group 1, but the fact remains that 1 in 10 did not have adequate shunts to reach adulthood. The medical-surgical team must weigh these odds and if at all possible allow the child to reach the most favorable Age Group 3.

In Age Group 3 (5 to 12 years) there are 32 per cent of the whole series and 16 per cent of the patients reoperated upon. Only 4 per cent of the patients in this group needed second operation, and 70 per cent of these were because the patient's growth during puberty had made the functioning shunt inadequate. These figures document forcefully the clinical teaching that this group has the best prognosis following operation.

In Age Group 4 (12 years and over) there were 16 per cent of the whole series and 12 per cent of the patients reoperated upon. Six per cent of the patients in this age group required reoperation. One-half of these had thrombosis of the shunts indicating a somewhat more difficult technical situation in this older age group. This fact lends support to the belief that a Potts anastomosis is probably a better initial procedure in this group, particularly since there was only one patient with a primary Potts anastomosis who required a secondary procedure and that was because the anastomosis was too large, not too small.

It has been repeatedly shown that, in the cyanotic group of patients, those with a tetralogy of Fallot can expect the most favorable long-term results from the systemic-pulmonary shunting procedures. In the first 1,000 of these 1,500 patients, 85 per cent were tetralogies and 80 per cent of them had good operative results.[3] A 5-year follow-up on the first 500 patients indicated a 70 per cent chance of maintaining this improvement in the tetralogy group but less than a 50 per cent chance for the other types of pulmonary stenosis with cyanosis.[4]

These data are not supported by the diagnoses present in this reoperated group in which one would expect to find a lower percentage of tetralogies as a reflection of their better prognosis following a first operation; but, in fact, 88 per cent of the patients reoperated upon were those with tetralogies. In the infant group, however, over one-third of the patients had diagnoses other than tetralogy of Fallot; this is perhaps a further explanation for the poorer postoperative results in this group.

Twenty-seven per cent of the patients reoperated upon had right aortic arches or about what would be expected in a normal tetralogy series. The side of the arch apparently did not influence the success of the first operative procedure.

It is of considerable interest that 9 patients in the group reoperated upon had end-to-end anastomoses originally and yet withstood temporary occlusion of the opposite pulmonary artery for the second anastomosis. One of the

condemning features of the end-to-end anastomosis has been the theoretic impossibility of reoperation if the shunt should thrombose because occlusion of the remaining pulmonary artery would block all output from the right ventricle. At least 8 of the 9 patients were thought to have shunt thrombosis, but all tolerated contralateral pulmonary artery occlusion during the second operation. These patients are thought to have had such severe pulmonary stenosis that the blood supply to the lungs was essentially by collateral systemic arteries and practically none from the right ventricle. For this reason bilateral occlusion of the main pulmonary arteries was well tolerated.

Another theoretic objection to the end-to-end anastomosis is the possible development of pulmonary hypertension in the isolated lung. Moderate elevation in pulmonary artery pressure has been produced experimentally by Dammann and Muller,[1] using an end-to-end systemic-pulmonary anastomosis to a single lobe of the lung, but there has been no clinical evidence of pulmonary hypertension in the patients in this series with end-to-end shunts who have been followed 1 to 8 years with an average of 3½ years.

The mortality rates for the secondary procedures have been reasonable in all but the infant age group, resulting in an over-all mortality rate of 9 per cent as shown in Table I.

The follow-up periods since the second operation as indicated in Table IV have a wide range in all 4 age groups but an average period of about 3 years. At the end of this period of follow-up 75 of the 83 patients evaluated were being treated as normal children or were showing satisfactory courses. This represents a good postoperative result in 90 per cent of those who survived the second operation.

There has been considerable interest in which type of shunting procedure should be used in patients who require second operations. There has been no established policy in this hospital. Careful comparison of the postoperative courses of patients with subclavian-pulmonary and aortic-pulmonary shunts revealed no statistical differences between the results obtained in the two types of anastomosis. The type of anastomosis has not influenced the generally good result from the second operation.

SUMMARY

Of the 1,500 patients with pulmonary stenosis and cyanosis who were operated upon between 1944 and 1957 at The Johns Hopkins Hospital, 109 required reoperation because their original systemic-pulmonary anastomoses became inadequate. The highest incidence of shunt failure occurred in the infant age group (0 to 2 years) in which one in every 7 patients required reoperation. The most common cause of a poor result in this group was thrombosis of the anastomosis. The best prognosis was in the 5 to 12 year age group in which only one patient in 25 required a second operation. The indication for a second anastomosis in 70 per cent of these patients was that they had outgrown their original shunts which were still patent and functioning well. Fifty-two per cent of the second operations employed a Potts-type anastomosis, but analysis

of the postoperative data indicates that the type of shunt has not influenced the generally good result from the second operation. Ten patients died during or shortly after operation, a 9 per cent over-all operative mortality. Eighty-three patients have been followed more than 3 months (average follow-up 3 years) since their second operation; 75 (90 per cent) of these are considered to have good postoperative results.

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REFERENCES

1. Dammann, J. Francis, Baker, James P., and Muller, William H.: Pulmonary Vascular Changes Induced by Experimentally Produced Pulmonary Hypertension, Surg., Gynec. & Obst. **105**: 16, 1957.
2. Ross, Richard S., Evans, M. H., and Taussig, Helen B.: Late Hemodynamic Complications of Anastomotic Procedures for Cyanotic Congenital Heart Disease. In press.
3. Taussig, Helen B., and Bauersfeld, S. Richard: Follow-up Studies on the First 1,000 Patients Operated on for Pulmonary Stenosis or Atresia, Ann. Int. Med. **38**: 1, 1953.
4. White, B. Daniel, McNamara, Dan G., Bauersfeld, S. Richard, and Taussig, Helen B.: Five-year Postoperative Results of First 500 Patients With Blalock-Taussig Anastomosis for Pulmonary Stenosis or Atresia, Circulation **14**: 512, 1956.

SURGICAL PHILOSOPHY

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I HAVE never talked on this subject and what I have to say is to an extent personal, for which I ask your indulgence.

What is the motivation for a medical student to choose surgery as a career? I have listed some of the reasons which surgeons have told me decided their course.

One reason is the desire to do something for the patient. Surgery is a form of therapy which gives a relatively quick answer. Most surgeons tend to be doers. Most physicians tend to be speculative, like to try out different remedies, and watch for effects. The more complicated the problem the better from the medical viewpoint. The surgeon likes to make a direct attack on the disease process.

Some surgeons have been influenced by teachers or doctors known to them in their student days (hero worship). An example is William Halsted, Professor of Surgery at Johns Hopkins Medical School who had a tremendous influence on surgery. Recognition of his outstanding qualities came when his pupils carried his teaching to the new medical schools of the country. He stressed careful handling of tissues, controlled hemostasis, deliberate gentle procedures, avoidance of infection, fine suture material, and methodical aftercare. He was a scholar who knew surgery and studied his own cases to find ways to improve results. He took his problems to the experimental laboratory and worked all his life to solve his surgical difficulties. He profited from his mistakes by recognizing what to avoid the next time. His teaching was too advanced for medical students but all practicing surgeons who found time attended his clinics. Graduate teaching was his forte. His pupils became famous.

Harvey Cushing, one of Halsted's pupils, pioneer neurosurgeon and founder of a school of neurosurgeons, prided himself upon being, first of all, a physician—a "good doctor." He carried on the Halsted traditions in his surgery. He made many contributions to the physiology of the pituitary gland. He was an artist of no mean ability, a bibliophile who made a great collection of medical books, and a literary physician who worked hard to perfect his writings. His course in experimental surgery was a great inspiration to all students and undoubtedly sent many into surgery.

John Finney, an all-around general surgeon, trained at the Massachusetts General Hospital and later in Baltimore. He did not have the Halsted touch, was a rapid operator, using heavy suture material, and rather rough in handling tissues. He was an excellent diagnostician, a good teacher, and had a very wide

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experience and a huge practice. The qualities that impressed the students were his manliness, fairness, courtesy, and solicitude for people. He was interested in the student's welfare, gave excellent advice to them, and was like a father confessor to most. Princeton tried to get him as her president and the medical students as well as the townspeople petitioned him to remain in Baltimore.

Howard Kelly, gynecologist at Hopkins, one of the most talented, graceful technicians in surgery, made many contributions to his field. He was deeply religious and fanatic in his attacks on vice. He was an herpetologist who had a large living collection in his home. He pioneered in radium therapy. In addition, he wrote splendid biographic sketches of physicians.

These four men were the ideals for Hopkins men going into surgery—scholar, scientist, humanist, and technician.

Some are attracted to surgery because they like to use their hands. The handicraftsmanship and good coordination necessary to athletes, artists, woodworkers, and musicians are also prerequisites for the surgeon. Surgery means "hand workers" (*εργον-χειρουργία*). A few follow family tradition. Their father, grandfather, uncles and so forth were surgeons. Opportunity opens to change the direction of some medical students. Financial opportunity draws some to the profession. Nurses in the operating room attract some to surgical careers.

Once the decision is made to become a surgeon, what kind of training should be sought? The ideal type of training is through the Halsted residency system. This is a gradual progression under supervision from the more simple to the most complicated types of surgery. In order to attain facility in the operating room, the student must see and take part in many varied types of surgery. Surgery today is much more compartmentalized than formerly. We have surgeons who limit their work to neuro-, head and neck, thoracic, heart, orthopedic, urologic, plastic, abdominal, pelvic, rectal, peripheral vascular, eye, ear, nose, and throat surgery. In fact to reduce surgery to absurdum there is a trend to limit it in other ways, such as to the surgery of trauma, the surgery of neoplastic disease, the surgery of infants, and the surgery of geriatrics. There is no justification for this hair-splitting of surgery. The fundamental principles of surgery apply to each and every one of these subdivisions. The surgeon must learn to control blood loss, avoid sepsis, readjust fluid and salt balance, restore nitrogen losses, and preserve the physiologic functions as completely as possible. He must learn to be a good physician. This will enable him to make differential diagnoses, anticipate possible complications following surgery, and be cognizant that the patient is a human being with physiologic and psychologic reactions. He will be able to consult with his medical colleagues to determine whether operation is or is not indicated and whether if performed it will do the patient good or harm. The more subdivided a subject becomes the less the doctor tends to know about the whole individual. The medical student hesitates to question the specialist regarding his opinion and fails to make the examination or take part in it to learn how

the opinion is derived. This is a lost opportunity. Specialization tends to develop "keyhole" vision. Learn to look at the wide horizon and look up as well. During his training period the surgeon should learn to interpret x-rays. He should follow up the gross pathology with microscopic examination so that he may get experience in interpretation of future cases. A year spent in pathology and experimental surgery can be combined most profitably in the training of the surgeon. It is one of the absurdities of the present surgical qualification boards that *no credit* will be given for this year of pathology. Since the time of John Hunter, the surgeon supposedly learns physiology and pathology by studying the effects of his work. This was the great contribution John Hunter made to surgery. It determines whether a surgeon is an intellectual individual or a hacker and slicer only.

When the student in training learns to take the responsibility for determining the operation and takes complete charge of it without supervision, he is a finished product and can safely be turned loose in the community. Progression to the residency can come in a considerable variety of ways. The residency schools have different ideas of their own although the tendency to regimentation by the surgical boards creates a uniform pattern.

There are other ways of getting surgical training than through the residency system. Some physicians have gradually picked up the more simple surgery in their general practice. The state laws allow a graduate in medicine who passes the State Board examination to be qualified as a "physician and surgeon." It is surprising how much of the surgery in this country is done by general practitioners, osteopaths, and chiropractors. Coller reported that less than 50 per cent of the surgery in Michigan was done by qualified surgeons.

Apprenticeship to a recognized surgeon or to a clinic is another pathway to surgery. Such trainees tend to be more dependent, and some never gain the confidence to stand on their own feet.

When a medical student puts years of his life into training to become a surgeon he has a right to ask what attributes should be possessed by the surgeon who is responsible for his training.

What attributes should be possessed by the trainer of surgeons?

He should be born to parents who believed, practiced, and taught him the value of the old-fashioned virtues: honesty in dealing with his fellows, Christian spirit—do unto others as you would have them do unto you, understanding—recognition of other viewpoints, judgment—as near as he can arrive at by weighing evidence, sympathy—ability to understand behavior especially in illness, the value of work—taking your share in the world's problems, the value of play—to keep from becoming one-sided and stale, sense of humor—to help over the rough spots, self-control—a sign of maturity, and consideration of others. He should be a good teacher with ability to present material in simple terms from background of experience, knowledge, and wide reading and ability to evaluate the wheat from the chaff, hold and arouse interest, stimulate curiosity, and make his pupils think for themselves. His personality should be warm. "A character" or a showman is not necessary but the cold statistician type is

deadly. He should teach by example gentleness, sympathy, and firmness when necessary. He should be understanding, helpful. He should learn from and correct his own mistakes and impressions. He should be a student with his pupils. He should be truthful and humble because of his opportunity in a high position, not vain. Every one of his pupils should be given equal opportunity to develop regardless of race, color, or social position. He should give of himself in time, advice, and help. His door should be kept open to his staff. He should live his religion in his daily life. He should put aside prejudice, envy, avariciousness, and infantile reactions. He should rise above flattery and adulation. He should walk in the path of truth.

The pupils should be given opportunity and material. They should be taught self-expression, not turned out in the same mold but each fitted according to his temperament. They should be given confidence in their own ability to do surgery as well as anyone else because of their sound basic training. The teacher can often funnel his pupils into their best direction for success in life—the extrovert into urology, the soft appealing baby type into gynecology, the strong football type into orthopedics, and so forth.

This paragon of perfection does not exist, but it is nice to think that he may.

What do we mean by surgical philosophy? The surgeon knows or should know that when he makes an incision he has damaged the body no matter how gentle and careful he has been. The area will never be the same again. No normal person wants his body marred by scars or multilated by having parts removed. Some psychopathic individuals, on the other hand, get satisfaction by having operations performed on themselves. Surgeons must learn to estimate the realities in these cases and do their best to avoid putting one more scar on the battleground. The justification for surgery is apparent when it is the surgery of necessity, such as severe trauma, hemorrhage, perforation, obstruction, gangrene, or malignancy. It may not be quite so evident when it is the surgery of election, after medical treatment has not been successful as in duodenal ulcer, regional enteritis, ulcerative colitis, or in uncomplicated diverticulitis, hypertension, quiescent infection, or stone in biliary tract, or benign tumor, or for cosmetic purposes. The surgery of prevention or prophylaxis is another category where the justification should be under scrutiny. Some such operations are tonsillectomy, appendectomy, polypectomy, and removal of skin or breast lesions. The surgery of palliation must be carefully evaluated from the point of view of time, severity of the surgical attack, and the promise of relief. In other words, except for the surgery of necessity, the surgeon must carefully weigh the advantages against the possible results and possible complications. This amounts to the actual estimation of calculated risks. Just because a surgeon has been trained to use his techniques in an expert manner is no reason why he should make use of them indiscriminately. He should not be scalpel-happy. He should think of his patient and question whether everything has been tried that might make it possible to avoid surgery. When he is convinced and his medical confreres agree, then the prospect

should be presented fairly to the patient and his relatives. It is not fair to them to ask that they make the decision. They are in no position to do this since they do not have the background to weigh the evidence. The surgeon must take the responsibility himself. The risks are his and the outcome depends upon his skill and the reaction of the patient to it. These he must be able to estimate. The patient and his family put their trust in the surgeon. They become dependent upon him and, if he is successful in his treatment, they often continue depending upon their surgeon for advice in many things. It is a measure of the surgeon's success to have this family-doctor relationship. He is regarded by them as their doctors were in days gone by. If, perchance, the surgeon is not successful in his treatment, provided he has been fair to those concerned, they will accept the outcome. The surgeon himself at such a time undergoes a soul-searching. Has he made any mistakes in his surgery? Will he attempt this type of operation again? Can he correct anything that he may have overlooked? These are the times when a post-mortem examination is sought by the surgeon and welcomed for what it may show. The unexpected pulmonary embolus, hemorrhagic pancreatitis, or hemorrhage into the brain may bring solace to him. But leakage from an anastomosis, peritonitis, or irreversible shock from too extensive a procedure leaves scars on the surgeon. It is especially hard for the surgeon when personal friends come to him and place themselves in his hands with confidence that everything will be all right. This is one reason why a surgeon should not operate upon his own family; it is harder for him to be relaxed at operation and devastating if a fatality occurs. There is an impression that surgeons must be hard in order to stand their daily occupation. But I can assure you that it is not so. Many surgeons are quite sensitive but they must become controlled or they cannot continue. I have frequently been asked by lay people, "how can you sleep after doing the things you have to do every day?" I can sleep because I am tired and because I come home only after I am sure that everything I know has been done to get a good outcome.

The surgeon must stand on his own in deciding whether operation is indicated in a certain situation. He should not be a handmaid to a physician who directs him to operate. This means that the surgeon must know a reasonable amount of medicine and at least some of the refinements in diagnosis. In some fields, such as surgery of the heart, at present, there is a team doing specialized tests to determine the suitability of each individual for surgery. In this field the surgeon cannot be present when all the tests are being done. But his colleagues must educate him and he in turn must keep them informed on cardiac surgery as done in other places. The surgery of the heart will for some time be a specialty limited to a few surgeons who will devote their time to it and do nothing else surgically.

In most surgical operations, the surgeon must strive to leave the patient with the best physiologic function that he can. When such a vestigial organ as the appendix is concerned there is no problem. Even the spleen has been regarded as practically without function and its loss can easily be compensated.

Removal of the gall bladder is followed by dilatation of the biliary duct system, thus in some measure taking over the function. Removal of one of paired organs such as the kidney is followed by hypertrophy of the remaining organ. Much of the stomach can be removed without upsetting the digestive function but total gastrectomy is often followed by a miserable period of convalescence. Removal of the pancreas makes much less trouble than would be expected. Large portions of the small bowel and all of the large bowel can be removed without noticeable effects when occasion demands it. The liver is notorious for how much of it can be removed with the small normal remainder functioning perfectly to keep the physiologic balance. The hyperfunctioning thyroid will regenerate quickly if too little is removed at operation, and if too much is removed myxedema will occur unless thyroid tablets are supplemented for the deficiency. Loss of sexual function may follow orchiectomy, ovariectomy, hypophysectomy, adrenalectomy, or removal of sympathetic nervous system tissue. Surgery for ulceration in the gastrointestinal tract can be staged and operation done at different times if occasion demands it. The surgery for malignancy is in a different category. The diagnosis of malignancy must be sure and this in most instances calls for biopsy and pathologic examination of tissues. There are very few exceptions to this rule. One is for cartilaginous tumors which can be diagnosed usually by the x-ray picture. Another is for pancreatic malignancy which as often as not gives no positive tissue for diagnosis. In these cases the surgeon should proceed as if dealing with malignancy unless from his experience he can make a diagnosis between chronic pancreatitis and cancer. When once the diagnosis of malignancy has been made surgery must be as radical as is consistent with getting well around the growth and its extensions. En bloc dissection of the focus with all the intervening tissue and the draining nodal area offers the best chance for cure. Less radical attacks may lead to recurrence or spread of the malignancy and the surgeon must at times sacrifice function hoping to find ways of overcoming the difficulties later. The first operation in malignancy should be radical and complete. Subsequent recurrences make succeeding operations less likely to be successful.

The surgeon should establish good rapport with the patient, his relatives, and friends before operation. If the patient's condition is not critical, he will often be reassured if his surgeon explains how his diagnosis has been made and what operation will mean. Some patients like to have their x-rays shown to them and their lesion pointed out. When the patient is in serious condition, his relatives and friends should have the explanation made to them. When there are a large number of brothers and sisters, the doctor can save time and trouble by asking them to appoint a spokesman for their group who will convey to the others the information the doctor gives. The same should hold for the house staff; trouble should be avoided by having a uniform report made instead of several different ones.

After operation, the surgeon should see the family and tell them what he found and the outlook. If complications occur after operation, the surgeon should take some of the family into his confidence and explain the situation

to them. He should keep them informed on the progress of the patient. He should willingly consent to consultation if the family is dissatisfied and he will be in a stronger position if he suggests consultation himself. His attitude should be one of sympathy for them in their time of worry. The priest and the physician have much in common in times of trouble. The Hippocratic school was founded in a temple and the treatment was for both soul and body.

The question often arises as to how much should be told the patient. This varies. What should the surgeon tell the patient or his relatives? Sometimes it is very important for the patient to know exactly what the surgeon thinks regarding his condition. He may be planning a long trip which the surgeon should not allow him to take if a dangerous delay will occur. Sometimes he may have a bad prognosis, in which case he may want to straighten out his affairs. He may wish to modify his will. He may want to arrange the succession in his business. He may want to have his children come home if possible.

If the patient is intelligent, he will want to know what the surgeon has done. He should be told in simple terms what the surgery has been. "We took out the diseased tissue." "We repaired the area so that it will function in a normal way." "We could not remove the diseased area because of danger to your life if certain structures were taken away. We made a bypass around so that normal function will be resumed." "You had a cancer but to our best examination, it had not spread and we think we got it all." "You had a condition about which we do not know any treatment." "We will try to help you in every way we can." "Something new may be discovered and we will remember you in such a case." "We will see to it that you do not have to suffer pain." "We will have to wait for microscopic sections."

It is important that the patient be allowed to convalesce without worry in the immediate postoperative period. This is a bad enough time in re-establishing normal function without having additional mental upset interfering. In such instances, I advise the patient to wait until he feels better unless I can give him very good news like "you did not have cancer as we feared," or "everything went very well and you should recover promptly." I have found that telling patients about their surgery in the immediate postoperative period is frequently not understood or remembered. There is a blackout especially when the patient has been critically ill. After the recovery the patient remembers nothing of the time when his life was hanging in the balance. The surgeon is not so fortunate. I have struggled and worried over medical colleagues who told me afterward that they remembered nothing at all of the critical time.

Should the patient always be told that he has an inoperable condition? I do not think so. Some want to know and, if they ask, you must tell them sympathetically without bowling them over brutally. In this area the surgeon is more than a doctor; he is a minister or a priest as well. It must be like an ecclesiastic giving solace to families or to sinners. It is surprising how well the average person accepts a calamity. I have been struck by the courage and philosophic attitude of the patient who knows that he has little hope left.

Some are grateful and try to cheer up their families and friends and even the doctor who has had to bring them bad news. Some live to the full in the remaining time alloted them.

The patient can be told that many people go around daily with inoperable conditions which will take their lives ultimately, such as the sudden injury in traffic, the bad cardiac, the hypertensive, the nephritic, the bad diabetic. Misery loves company and we all have plenty of both.

The surgeon is often in a dilemma because he is asked, "How long will I live?" He cannot tell. He can say that the average length of life in this certain type of disease for a big group of people is so much. But some people die early and others last much longer than the average. How can he say what each individual will do? In other words, you are dealing with individuals and not groups of statistics. This individual may be at either end of the statistic group.

Some patients cannot stand adversity. If told that they have an inoperable condition, the remaining time becomes a misery to them. They fold up and never have another good minute. The sword of Damocles hangs heavily over them. Let them enjoy what time they can in relative comfort. Tell some responsible relative the truth as you see it. Tell him that all the family must conspire to make the time pleasant and comfortable to the patient as long as they can. And when it finally becomes necessary to tell him, let the doctor and the minister work together.

Many patients never know and never ask about their chances. Other patients know and never ask. Others know and ask the doctor to keep it from their families. The good physician estimates the effect of bad news on the whole family and sometimes withholds his information especially when others in the family are also ill.

When you talk to a woman about a lump in her breast, you tell her that a biopsy must be done. If the microscope shows a benign lesion, a local removal is all that will be necessary. It the lesion is malignant, the whole breast must be removed. Every such patient who awakes after a mastectomy knows she has malignancy. Many never ask anything about it. Others want to know if it has spread. You tell them to the best of your knowledge after careful microscopic examination. The convalescence will be long in any case and many recurrences do not come until the second or third year after operation. The surgeon should give them assurance that they will be carefully followed and that they will not have any trouble for some time in any case. Thus, they can "travel hopefully." As Stevenson says, "It is better to travel hopefully than to arrive."

The surgeon and the physician will encounter inevitably, at some time, people who become unreasonable. They are under emotional strain and they must release their tensions on somebody. They come to the surgeon and register complaints. "Our father, mother, etc. is not getting good care. Nobody gives him or her any attention. We want special nurses around the clock. The food is bad. Your treatment is not right." The surgeon must listen patiently.

He must not lose his temper although he has worked "like a dog" on this case. He must explain the workings of a big hospital; how care is apportioned as best we can; how nurses are scarce, all being married to medical students or doctors; how the food is fitted to the stage of recovery or the necessary diet of the patient; and finally if they are dissatisfied with the surgical care perhaps they would like to get some other surgeon in consultation. Of course, a surgeon from the Mayo Clinic or New York or Boston is a high-priced commodity. Perhaps, the family lacks confidence in their surgeon, in which case he will be glad to hand over the results of his investigation and opinion to some other surgeon whom he approves. This usually cools them off.

Surgical fees should be reasonable. The days of gouging the patient for "all the traffic will bear" are gone. Most surgical fees are now set for the insured and certainly should not be a hardship for most people. The mink coat and Cadillac group should certainly not resent being charged a little more than the set insurance fees, although some of them may be "big fronts" who are really deeply in debt. Surgery should never be regarded as a commodity like Quaker Oats or onions to be purchased over the counter at a fixed price. The surgeon is not or should not be in a trade. Surgery is a profession. It is not as smart as the legal profession which would not allow anyone to set prices for their skill. When the surgeon operates on a public figure in the community, it is worth more because he is under public surveillance. Many people want information regarding the prospect of the patient's return. Perhaps the stock market will break if he suffers a complication. And if by ill luck he should die, perhaps because of a pulmonary embolus, the surgeon may lose reputation. On the other hand, when the patient recovers because of his own natural resistance, the advertising value for his physician is inestimable.

Professional courtesy is given by the surgeon with no charges to his colleagues, nurses, and the clergy.

The surgeon must try to eliminate his specialty. Some day this may be true for infections and for neoplastic disease. I do not think that trauma will ever be abolished as long as man has high-speed machines and is careless in their use.

The millennium will be achieved when the surgeon no longer needs his cup of black coffee, spiked with rum, and three iron doughnuts to keep his courage up. Perhaps in the future he and his medical colleagues can lounge back and sip weak tea and eat ladyfingers after he gives his patients the needle or a handful of pills. That will be the day!

COMPARATIVE STUDIES WITH A NEW PLASTIC SURGICAL MASK

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THE importance of airborne invaders in the problem of surgical wound infections has been underestimated and generally neglected until recently. Evidence that some strains of bacteria (particularly *Staphylococcus aureus*) are resistant to any known form of chemotherapy has stimulated a re-evaluation of aseptic techniques with special emphasis on airborne contamination. Since surgical wound sepsis is initiated in the operating room in most instances, it seems reasonable to concentrate considerable effort at this point. It is the purpose of this article to introduce a new type of surgical mask which we, at Minneapolis General Hospital, believe to reduce significantly the threat of contamination of surgical wounds from the nose and throat of the operating room personnel.

METHOD AND MATERIALS

A comfortable, durable mask which would deflect the stream of expired air from the operative field was desired. Filtration of the bacteria-laden stream of expired air to prevent saturation of the air about the operative field with microorganisms was also considered important, for in this way secondary fall-out contamination could be minimized.

Facial impressions were made of several surgeons and operating room nurses, from which a common facial mould was developed. A plastic with suitable properties was formed on this mould, after heating, in such a manner as to allow free egress of expired air and at the same time deflect the stream of air away from the operative field. A filtering device of disposable material was then added to catch droplets as air left the side vents of the mask. Sponge rubber seals the edges of the mask and the skin of the face across the upper and lower margins. The Minneapolis General Hospital Surgical Mask thus becomes a closed system (note features of design in Fig. 1). Tests were then carried out to determine the efficiency of the mask both with regard to its capacity to deflect the stream of expired air and also to its ability to "filter" the moisture-laden air.

Pour plates of nutrient agar were held at a distance of one foot from the unmasked mouth and nose of an individual who was actively mouth breathing for a period of 5 minutes. At the end of this 5-minute period, the subject gave one short cough. This procedure was repeated 5 times and the individual agar plates were incubated for 24 hours. After incubation a total colony count was

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made and results were as tabulated in Table I, *A*. In the second series (Table I, *B*), the same procedure was repeated after the subject had been wearing a conventional, single, multilayered gauze mask for 30 minutes. In the third series (Table I, *C*), the subject had been wearing 2 conventional masks (double masking technique) for a 30-minute period. In the fourth series (Table I, *D*), the Minneapolis General Hospital Surgical Mask was substituted for the conventional mask. It was obviously impossible either to cough or to breathe on a plate held directly in front of the face while this mask was worn and the few colonies

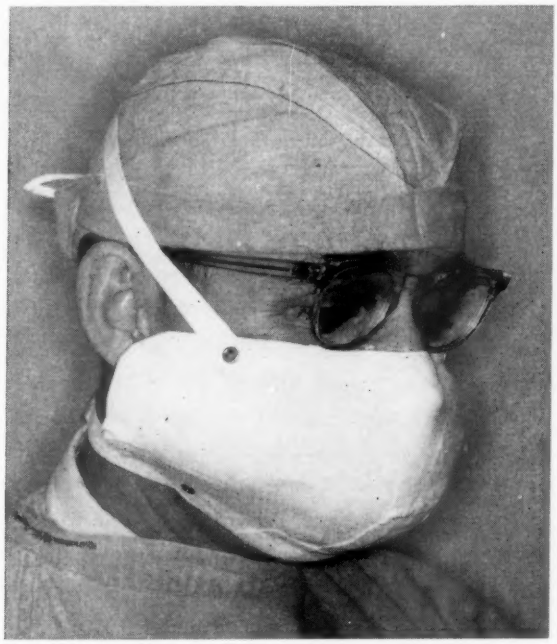

Fig. 1.—Minneapolis General Hospital Surgical Mask. Made of durable plastic and fitting snugly to the face with discharge of expired air through posteriorly directed side vents.

TABLE I. COMPARATIVE BACTERIOLOGIC STUDIES

	BACTERIAL COLONIES PER POUR PLATE*					
	TEST 1	TEST 2	TEST 3	TEST 4	TEST 5	AVERAGE COLONIES
A. No mask	Over 300	Over 300	Over 300	Over 300	Over 300	300+
B. Single conventional mask	121	184	153	104	161	145
C. Double conventional mask	34	68	41	29	46	43
D. Plastic mask—Minneapolis General Hospital type	2	0	0	3	1	1.2
E. Plastic mask—held 5 minutes at each posterior side vent	4	7	9	6	3	5.8

A, B, C, & D.—Pour plates held 12 inches from face for 5 minutes; normal mouth breathing plus 1 cough.

E.—Pour plates held 5 minutes 6 inches from side vents.

*Read after incubation for 24 hours.

growing in this group of pour plates were believed to be due to fall-out contamination of the room air. A fifth series of plates (Table I, *E*) was then used to test the efficiency of the filtering device, and pour plates were held 6 inches from each of the deflecting vents of the mask for a period of 5 minutes (10 minutes total exposure).

The data indicate a remarkable protection afforded by the Minneapolis General Hospital Surgical Mask over standard gauze masks—300 colonies with no mask, an average of 145 colonies with a single conventional mask, 43 colonies with double conventional masks, and 1.2 colonies with the new plastic mask.

DISCUSSION

When the surgeon directs his vision toward an open surgical wound which is bathed in serum, he is often aiming a veritable arsenal of disease into the operative area; and, when he speaks, he pulls the trigger and literally sprays the field with microorganisms. Better control of airborne droplet contamination is incumbent upon those involved in operating room management today.

As early as 1898, Hübner[1] recognized the potential danger of the respiratory tract of the surgeon as a source of secondary wound contamination. He later concluded that the gauze mask fitting tightly over the mouth became readily saturated and served as a reservoir for bacteria-laden droplets. These he demonstrated to be easily sprayed about even in the circumstance of complete cessation of speaking. Mendes,[1] in 1904, attempted to disinfect the mouth before operation, but he found this impossible with ordinary mouth washes.

In 1933, Hunt,[3] in a study of wound infections, concluded that mild infections were generally the result of dried and attenuated organisms which float in the air, while more serious infections usually could be traced to surgeons and other operating room personnel who harbored acute sore throats and contaminated the field by coughing, sneezing, or talking. Riese,[1] in 1936, again suggested the inadequacy of the conventional surgical masks; he concluded from his series of experiments that eleven-twelfths of all pathogenic organisms in surgical wounds were present as a result of speaking directly into the wound during surgery. It is little wonder that he is noted for having demanded absolute silence at the operating table.

Fischer and Petrick,[1] in 1950, subjected conventional multilayered gauze masks to a series of bacteriologic tests. They found that all masks diminished the spread of droplets but still allowed microorganisms to pass through during normal speaking. They found that whispering failed to modify the situation significantly.

With the recent increase in postoperative wound infections, Howe[2] (Massachusetts Memorial Hospital) and others have pointed directly at the problem. They have found positive cultures of staphylococci from the hands or nose of 99.2 per cent of operating room personnel and patients. Of these staphylococci 78.5 per cent were penicillin resistant. Howe attributes the increase in wound infections to the tremendously increased exposure of wounds to staphylococci. He recommends an increase in vigilance on the part of all

personnel in protecting themselves from becoming carriers and extreme care in the operating room to prevent passage of organisms from nose and throat to wound.

The Minneapolis General Hospital mask may be a valuable adjunct in this crisis of postoperative wound infections. It prevents direct contamination by speaking, coughing, or neezing and filters the expired air. It has been found to be comfortable during long operative procedures, and in no way hinders the vision or the mobility of the surgeon. It permits unhindered conversation (safely) at the operating table which is so important in training young surgeons. Fogging of glasses by warm expired air is avoided. It should be emphasized that this masking procedure is intended as a refinement of aseptic technique and in no way implies relaxation of any of the other principles of technique necessary for aseptic surgery.

SUMMARY

1. A brief discussion of some of the evidence incriminating the nasopharynx of the surgeon and operating room personnel as a source of secondary contamination of surgical wounds has been presented.

2. A new, durable, plastic surgical mask (the Minneapolis General Hospital Surgical Mask) is presented as an adjunct to aseptic surgical technique.

REFERENCES

1. Fischer, A. W., and Petrick, W.: Bedeutet die "übliche" Gesichtsmaske einen ausreichenden Schutz Operationswunde? Zentralbl. Chir. **75**: 895-902, 1950.
2. Howe, C. W.: Postoperative Wound Infections Due to Staphylococcus Aureus, New England J. Med. **251**: 411-417, 1954; quoted by Dineen, Peter, and Pearce, Charles: A Ten-Year Study on Wound Infections, Surg., Gynec. & Obst. **106**: 453-458, 1958.
3. Hunt, E. L.: Some Further Observations Upon Contamination of Operative Wounds by Airborne Bacteria, New England J. Med. **209**: 931, 1933.

THE FLIP SIGN IN SCIATIC NERVE TENSION

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THE flip sign is a test devised to demonstrate conclusively the presence or absence of sciatic nerve root tension. Not the least of its attributes is the fact that it does not require full cooperation of the patient, and it is of inestimable value in drawing with certainty the fine line of demarcation between the genuine and the counterfeit case of sciatic nerve tension. A case in point is the litigant with no significant neurologic changes of the lower members who will not flex the trunk on the pelvis nor permit elevation of the lower members beyond a few degrees, while in the supine position.

The mechanics of the flip sign are as follows. The patient is instructed to sit squarely on the examining table with his legs dangling off its side and to hold his back as erect as possible (Fig. 1). The arms hang at the sides of the body or may be used by the patient for supplemental fixation against the table of the thigh to be tested. The examiner places the open palm of one hand against the distal thigh (suprapatellar area) of the affected extremity, depressing the thigh against the table, and his other hand under the heel cord so that the heel rests in the palm (Fig. 2). The affected limb is then gradually extended at the knee. In cases of genuine sciatic tension no resistance or complaints are noted until the 45 degree arc is reached, but continuance of elevation past that point is attended with an acute reversal of the lumbar lordosis, and the patient tends to fall backward, frequently needing to brace himself against the table with his hands to prevent a complete backward fall on the table.

In cases of genuine sciatic nerve tension, when the flip sign is positive, it is noted that the individual is unable to sit erect on the table with both knees fully extended. There is either a flexion attitude of the knee of the affected extremity or a reversal of the lumbar spine with backward flexion position of the trunk to avoid the pain associated with nerve root tension. The simulator, with a negative flip sign (Fig. 3), rarely evidences any difficulty in sitting on the table in an erect position, with both knees fully extended (Fig. 4).

The test is both qualitative and quantitative. It is of value particularly in those cases of genuine sciatic nerve root tension where there are no significant neurologic manifestations, when it invariably is indicative of the presence of an L_4-L_5 lesion. Furthermore, because of its dimensions, we have found it to be the specific test for concluding diagnosis and also for prognosis in determining the course and progress in lower lumbar nerve root compression and tension. It

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has been our experience that surgery is indicated solely in cases where the arc of the flip sign has remained stationary or has become progressively increased. In cases where there are neurologic findings of the lower members but a negative flip sign (burned-out disc), surgery rarely accomplishes any benefits.

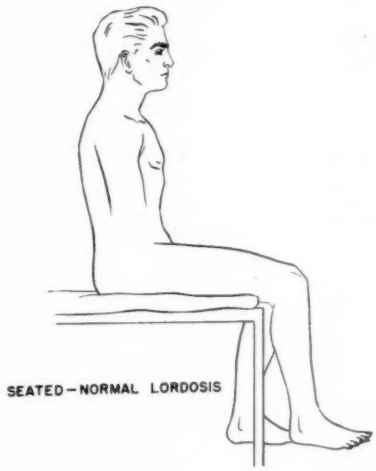

Fig. 1.

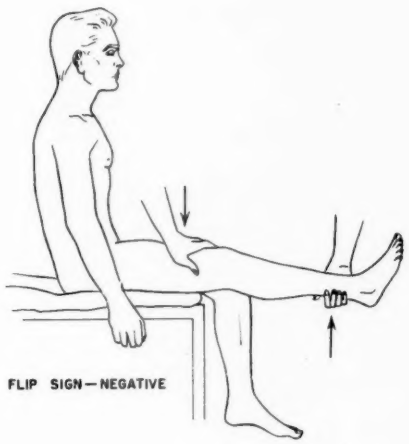

Fig. 2.

Fig. 1.—Patient sitting erect on the examining table, legs dangling off the table.
Fig. 2.—Positive flip sign is present when the examiner depresses the distal thigh against the table with one hand, with the other gradually elevating the heel with extension of the knee, producing a reversal of the lumbar lordosis with backward flexion of the trunk.

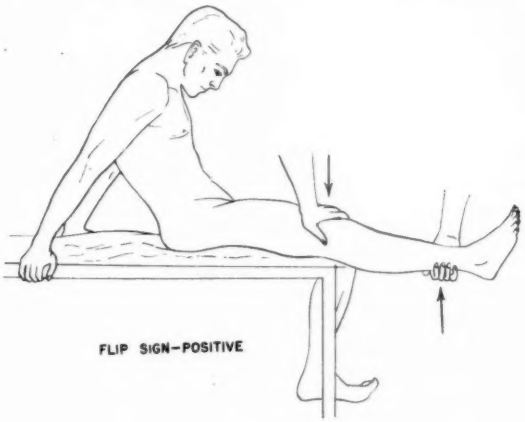

Fig. 3.

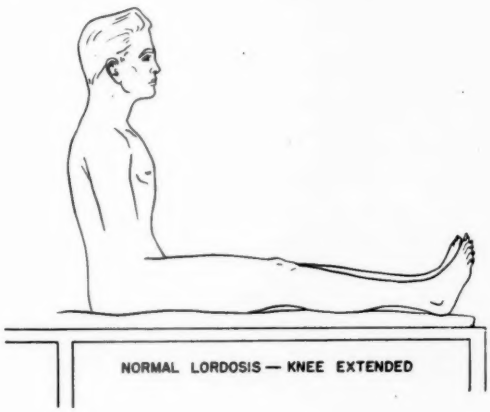

Fig. 4.

Fig. 3.—Patient with negative flip sign, knees extended and spine erect.
Fig. 4.—Confirmatory test for negative flip sign; spine erect, both knees extended.

The flip sign test is performed routinely as a confirmatory finding following the straight-leg-raising test on the affected extremity. The arc of positive elevation in straight-leg raising is the same as the arc of elevation in the flip test, when reversal of the lumbar lordosis commences. Sciatic nerve root tension has been proved in more than 95 per cent of cases that have come to surgery over the past 5 years.

The test may be found to be positive in both lower members in cases of (1) bilateral hamstring contractures, (2) acute central type of herniated lumbar

intervertebral disc, and (3) acute, advanced lumbosacral derangement. In the first type, differential diagnosis will indicate the postural spinal flexion and dorsiflexion of the ankle defects consistent with bilateral hamstring contracture. The acute central type of lower lumber herniated intervertebral disc can usually be demonstrated clinically without the use of the flip sign, and the acute advanced lumbosacral derangement will manifest itself by other signs and tests.

SUMMARY

The flip sign is introduced as a reliable and simple method of determining the presence and extent or absence of sciatic extrathecal nerve root compression or tension. It is of immense value in detection of the simulator.

Appraisal of Progress in Surgical Therapy

CONDUCTED BY WARREN H. COLE, M.D.

AN APPRAISAL OF THE TREATMENT OF GASTRIC ULCER

CLAUDE E. WELCH, M.D.,* AND JOHN F. BURKE, M.D.,** BOSTON, MASS.

VARIOUS controversies attend the treatment of gastric ulcer that are much easier to formulate than to resolve. In fact some statements made in the literature are so dissimilar that it may seem hopeless to extract any semblance of agreement, while data from some institutions, presented by different groups, may show wide variation in factual material and conclusions.

The important differences of opinion involve two related problems, namely, the relative efficacy of medical versus surgical therapy of gastric ulcer and the frequency of confusion of gastric cancer with ulcer. They are abetted by an elastic definition of cases that are included in the category of gastric ulcers. Such lesions can, by the microscope, be segregated accurately into various groups. Most important of all of them—the so-called peptic ulcer of the stomach, devoid of any evidence of malignancy—is a pathologic entity, and it would be fortunate if the discussion could be confined to this particular disease.

Unfortunately, however, the physician cannot see with the eye of the microscope and, unless a retrospective study is made, a more liberal interpretation of the gastric ulcer becomes necessary if the discussion is to be significant for the clinician who is concerned with diagnosis and treatment. The most important lesions that must be considered include these associated diseases: (1) the chronic benign gastric ulcer, (2) the gastric ulcer that is benign by all clinical criteria, while the microscopic examination proves it to be malignant (known also as the "ulcer-cancer" or malignant ulcer), (3) gastric ulceration that occurs in an overt cancer, lymphoma, or spindle-cell tumor, and (4) acute superficial gastric ulcerations.

Accurate segregation of these groups would be desirable. However, it is clear that insertion of a given patient into one of these groups must depend upon several items of evidence, not all of which necessarily point to the same conclusion. In the same fashion, the radiologist must balance evidence; he may believe a certain ulcer has a 90 per cent chance of benignancy and another

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only 60 per cent. Obviously, statistical data derived from conclusions based upon opinions essentially are still matters of opinion rather than valid mathematical statements.

Because of this inability to segregate the 4 groups sharply, many of the discussions on the relationship of gastric ulcer and cancer have included data from all ulcerative lesions of the stomach as a basis for statistical conclusions. For example, Holmes and Hampton[10] in 1931, following this conception, stated that 90 per cent of all prepyloric ulcerations were malignant. Because of improved diagnostic techniques, it is apparent at present, when all prepyloric ulcerations are considered, that the occurrence of cancer is well below 50 per cent. However, when overt cancers are excluded from consideration, a far different figure is obtained, for only 5 to 10 per cent of apparently benign prepyloric ulcers now are found to be malignant.

This point is stressed because it furnishes the most logical explanation for the variable conclusions recorded in the literature. By the same token, since it is impossible to examine minutely the data from which these conclusions are derived, any attempt to resolve those differences in this or any other critical survey cannot be entirely successful. It would seem much more appropriate to support our opinions by an examination of our own most recent data, supplemented by certain other applicable material from other clinics.

The questions that are most appropriate and which should be answered insofar as possible are these:

1. What is the magnitude of the ulcer-cancer problem, and how does it influence methods of diagnosis and therapy?
2. What are the indications for operation for the gastric ulcer that is believed to be benign?
3. What is the proper operation for gastric ulcer?
4. How is the choice of treatment influenced by follow-up studies?

While these questions are closely interrelated, insofar as possible they will be considered separately.

For the purpose of this paper, data have been secured on 367 patients seen in the Massachusetts General Hospital during the years 1952 through 1957, inclusive, in whom the diagnosis of benign gastric ulcer was made. Two hundred and twenty-one (60.2 per cent) of these patients had an operative procedure and the diagnosis was confirmed in 205, while, in 16, gastric cancer was found. One hundred and forty-six were not operated upon and 6 of them died. In the others who had medical therapy and survived, the ulcer was believed to be benign because of the clinical course. Follow-up studies were not extensive enough to warrant the statement that they all actually were benign, and two were proved later to have cancer of the stomach at autopsy. However, it does not seem reasonable to believe that many cancers actually were overlooked in this way.

Before discussing the specific questions outlined above, some items of general information may be summarized briefly. Fifty-seven per cent were men; their ages varied from 18 to 86, with a median of 59. Insofar as symptoms were concerned, 311 patients complained of pain, 64 of nausea, 152 of vomiting,

77 of hematemesis, and 95 of tarry stools. The symptoms were of less than 1 day's duration in 22, 1 day to 1 week in 20, 1 week to 1 month in 39, 1 to 6 months in 61, 6 months to 1 year in 44, 1 to 2 years in 23, 2 to 3 years in 24, 3 to 5 years in 17, and over 5 years in 99.

The interpretation of various diagnostic studies may be summarized as follows. The radiologist's opinion was recorded in 299 examinations. The ulcer was believed to be benign in 243, either benign or malignant in 56, and no ulcer was seen in 22. The location of the ulcers is shown in Table I.

TABLE I. LOCATION OF ULCER

Lesser curve	3
High	33
Mid	70
Antrum	67
Prepyloric	35
Pyloric	60
Fundus	5
Posterior wall	10
Greater curvature	3
Duodenal (gastric ulcer not seen)	10
In hiatus hernia	1
No ulcer seen	22
No x-ray in this hospital	45
Location not noted	5
	366

In this table, the location of the gastric ulcer as determined by x-ray is shown. Of the 299 patients who had a gastric ulcer in this hospital 46 also had a duodenal deformity or an active duodenal ulcer.

Gastroscopy was carried out 51 times. The ulcers were visualized and the diagnosis was correct in 23 instances, the question of cancer was raised in 6, and the examination was unsatisfactory or the ulcer not visualized in 22.

Gastric analysis was done in 160 patients. True histamine achlorhydria as recorded by Topfer's reagent was present in 14.

Cytologic smears were carried out in 187 patients. They were unsatisfactory in 24 and doubtful in 9. One hundred and forty-eight were read as negative, and of this group 2 patients had cancer. Six were read as positive, and of this group 3 patients were proved to have benign ulcer and 3 cancer on pathologic examination of the resected specimens.

These preoperative studies emphasize the impossibility of the differential diagnosis of ulcer and cancer, a fact that has been elaborated upon in the past by many authors.[12, 24] Of all methods available, the radiologic examination is by far the most reliable.

THE ULCER-CANCER PROBLEM

In 1940, Mallory[13] subscribed to the view that gastric cancers originated de novo and did not arise from pre-existing benign ulcers. According to his opinion, any cancer of the stomach may be subject to peptic ulceration, but particularly when the cancer is of a low grade the carcinoma may be nearly completely destroyed by secondary ulceration and then closely mimic a benign ulcer. He demonstrated the existence of cancer in situ in the stomach that by clinical observation has been shown to have a relatively slow rate of growth.[26]

We have subscribed to this point of view, but it must be admitted that many pathologists still believe a small percentage of gastric cancers arise from previously benign ulcers. It is apparent that neither thesis is susceptible of proof, since total excisional biopsy would be necessary at numerous stages throughout the life of a given ulcer, for in no other way could cancer be ruled out completely and total biopsy would, of course, interrupt the experiment.

The important clinical feature is the determination of the number of ulcerated cancers that mimic benign ulcers. It is apparent from the previous discussions that this figure can be only an approximate one, but it does seem clear that the problem is less important in our institution than it was a decade or more ago.

In 1941 Allen and one of us (C. E. W.)[24] found that this figure in our hospital was approximately 14 per cent. In 1947 it was near 10 per cent.[25] In the present series, of 367 patients believed to have benign ulcer, only 18 (4.9 per cent) were proved to have cancer. When the 221 patients who had gastric resections are considered, 16 (7.2 per cent) had cancer. Only 2 of 146 treated medically were known to have developed cancer later. Manifestly this is an incomplete follow-up but even if they developed cancer in the same proportion as those who had surgery, the figure becomes less impressive than it was in the past.

The suggestion that all gastric ulcers should be treated surgically, based upon the frequency of misdiagnosed cancer, was championed originally by Lahey[11] in 1947, although he later became somewhat less rigid in his views. It has been supported vigorously since then by many surgeons including Ochsner,[16] Ravdin,[17] and Strode.[20] The original argument in favor of this point of view was that differentiation of gastric cancer from ulcer was impossible in x per cent of patients, and death from resection of ulcer occurred in y per cent; when y became less than x there would be a definite advantage in favor of resection for all gastric ulcers.

This simple mathematical formula has required modification since cure of the cancer cannot be expected in all cases even with early resection. The 5-year survival figure of gastric cancer diagnosed preoperatively as benign ulcer, after resection, in our series is now 50 per cent. Furthermore a few of the patients with benign disease will be incapacitated after operation wherein disability due to postgastrectomy symptoms has been substituted for the symptoms of ulcer.

The mortality of gastric resection for benign ulcer is and probably will remain for many years throughout the country at a level far closer to 5 than 1 per cent, since gastric ulcer is a disease of middle and old age and the average age of our population is increasing. Furthermore, many of the ulcers are manifested by massive hemorrhage which has a high mortality. In our hospital the mortality of resection for gastric ulcer was 3.0 per cent in the years 1940 through 1946, and it is 3.6 per cent in this series (Tables II and III). The operative mortality in the Mayo Clinic in 1955 was 2.5 per cent. Probably more typical of the country as a whole is Watman's figure of 7 per cent from the Ohio State University Hospital.

TABLE II. MORTALITY ACCORDING TO TYPE OF THERAPY FOR GASTRIC ULCER
(Massachusetts General Hospital, 1952-1957)

TYPE OF TREATMENT	TOTAL NUMBER OF PATIENTS	TOTAL NUMBER OF DEATHS	PER CENT MORTALITY
Surgical	221	8*	3.6
Nonoperative	146	6	4.1
	367	14	3.8

*Five of these deaths occurred in 47 patients operated upon for acute massive hemorrhage.

TABLE III. CAUSE OF DEATH AFTER OPERATION

AGE	INDICATIONS FOR OPERATION	CAUSE OF DEATH	FINAL DIAGNOSIS
65	Gallstones; ulcer at operation	Pulmonary embolus	Carcinoma
64	Hemorrhage while under treatment	Pneumonia	Carcinoma
64	Massive hemorrhage	Peritonitis	Benign ulcer
49	Massive hemorrhage	Pulmonary embolus	Benign ulcer
73	Massive hemorrhage	Subdiaphragmatic abscess	Benign ulcer
76	Massive hemorrhage	Pulmonary edema	Benign ulcer
63	Failure to heal (Hb. 10 Gm.)	Pulmonary emboli	Benign ulcer
83	Probable cancer with hemorrhage (Hb. 5 Gm.)	Thrombosis renal artery	Benign ulcer

Deaths in all instances followed partial distal gastrectomy.

These figures are cited in detail since by such a method it appears clear that the opinion stating that all gastric ulcers should be subjected to surgery cannot be predicated solely on the danger of cancer. For example, in our hospital if 100 patients with supposed benign ulcer were subjected to operation, between 5 and 10 would be found to have cancer. At the end of 5 years considering an operative mortality of 3 per cent and a 5-year survival rate of 50 per cent for the ulcer-cancer group, 92 to 95 patients would be alive, of whom 3 or 4 would develop recurrent ulcer or have severe postgastrectomy symptoms. On the other hand, if all patients with benign disease could be treated successfully by medical measures and none were operated upon, at the end of 5 years all patients with cancer would be dead, but 90 to 95 would still be alive.

It follows from this analysis that it is reasonable to treat some patients with apparently benign ulcer medically, although, if so, the utmust care must be taken to refer those who have cancer for early operation. In this regard it is probably unnecessary to point out again the fallibility of all known methods of differential diagnosis of ulcer and ulcer-cancer. However, at present we believe that some cases can be singled out for immediate operation and that others may be given a trial of therapy; operation is carried out because of failure to heal or recurrence thereafter. By these methods we believe few cases will be overlooked. Some surgeons maintain that a short period of observation introduces sufficient hazard to be undesirable; we believe 10 to 14 days can be devoted to such treatment without significant danger.

A report from the Mayo Clinic by Cain and co-workers,[2] should be emphasized here since it shows that differentiation of the benign and malignant ulcer by the physician is little more accurate than selection by choice.

Their series of 414 patients with supposed gastric ulcer was treated medically and then followed 5 years later. Seventy-eight of this group had medical

therapy because they refused surgery; 12.8 per cent were known finally to have had cancer. The other 336 had medical therapy because the clinic physician believed it to be safe and satisfactory, but, at the end of 5 years, 9.8 per cent of these patients were known to have had cancer. A great deal of doubt, therefore, is cast upon the physician's ability to differentiate the diseases of gastric ulcer and cancer any more accurately than the patient can. It does seem fair to suggest, however, that an accurate follow-up at short intervals, might have directed many of these patients to the surgeons at an early time opportune for cure.

INDICATIONS FOR OPERATION

While the inability to differentiate gastric ulcer and cancer thus is a rather tenuous indication for surgery in all cases of supposed benign gastric ulcer, there are numerous other indications that are even more cogent to support the validity of surgical therapy. The chief indication for operation in each patient is given in Table IV and will be discussed briefly.

TABLE IV. INDICATIONS FOR OPERATION FOR GASTRIC ULCER

OPERATION	NUMBER	PER CENT OF OPERATED CASES	PER CENT OF ALL CASES
Chronic pain	94	43	25
Bleeding			
Massive	47	21	13
Chronic	16	7	4
Possible cancer	32	14	9
Obstruction	13	6	4
Perforation	5	2	1
Erroneous diagnosis	2	1	1
Not recorded	12	6	3
No operation	146		40
Total	367		

1. Chronic pain, flatulence, heartburn, nausea, or vomiting relieved partially or intermittently by medical therapy led to nearly half of the operations. One hundred and twelve patients had evidence of gross or occult bleeding at some time of their hospital course. When all patients with gastric ulcer are considered, about one-quarter of them prove intractable because of persistence of these symptoms.

2. Hemorrhage is a very important reason for operation. The tendency for bleeding from gastric ulcer to be massive when it once begins and the high mortality attendant upon such bleeding have been stressed repeatedly. In a previous study from this hospital,[23] in which the mortality from hemorrhage was studied in the years 1954 through 1955, gross bleeding (demonstrated by hematemesis or one or more tarry stools) from a gastric ulcer was observed in 34 cases. Of these, 29 patients had severe hemorrhage by demonstrating a fall in hemoglobin to 7 Gm. or lower or by demanding 2,500 c.c. or more of blood while under therapy; only 2 had moderately severe hemorrhage as manifested by a fall in hemoglobin to no less than 10 Gm., and only 3 had mild bleeding. The mortality of all patients with gross hemorrhage was 11.8 per cent and of massive hemorrhage 24 per cent.

When the material in the present study is considered, nearly one-third of the operations, representing 17 per cent of the total patients, were necessitated by hemorrhage. Furthermore, the postoperative mortality following resection for gastric ulcer is confined nearly entirely to those patients who have severe degrees of anemia or who are operated upon for massive hemorrhage. The mortality in the absence of severe hemorrhage or anemia was 1.9 per cent, since 3 patients died of 154 who had surgery; in the presence of severe hemorrhage or anemia 5 of 47 patients died (10.6 per cent).

3. Inability to exclude cancer was the major indication for intervention in 15 per cent of the patients with operations. Failure to heal under therapy, recurrence of the ulceration at a later date, gastric ulceration with histamine achlorhydria, or positive cytologic smears of the gastric washings in the presence of apparently benign ulcers were the main reasons for inclusion in this category.

4. Of the other indications for operation it is of interest that obstruction or perforation, two of the common complications that lead to operation for duodenal ulcer, are much less important with gastric ulcer. Complete pyloric obstruction in the presence of a known gastric ulceration is usually proved to be to cancer. Perforations in the pyloric area are excluded from consideration since they nearly always are duodenal rather than gastric, while perforations along the lesser curvature are comparatively rare. The preferable therapy of either obstruction or acute perforation is gastric resection, although plication with local excision or biopsy of the wall of a perforated ulcer is still carried out in poor-risk patients.

5. The size of the ulceration is important since cancer becomes increasingly common with increasing diameter. However, large benign ulcers are encountered not infrequently. Turner and associates,[22] found that 4 per cent of all benign gastric ulcers observed in the Mayo Clinic from 1940 through 1954 were 4 cm. or more in diameter. These large ulcers may be manifested by all the signs of malignant disease, such as persistent epigastric pain, severe loss of weight, gastric hemorrhage, and an epigastric mass.

6. The location of the lesion now is considered to be relatively less important than it was in the past. There still seems to be an increased incidence of cancer in the distal stomach, but benign ulcers occur nearly as frequently as they do higher on the lesser curvature. Examples of benign ulcerations along the greater curvature continue to appear although they are relatively uncommon; there were 6 in this series, and nearly 100 have been recorded in the literature.

These indications furnish a rough guide to selection of the type of therapy. Early operation is indicated whenever the appearance of the lesion, either by x-ray or gastroscope, is suggestive of cancer. It is also indicated when the ulcer appears benign by x-ray and the patients have had either a long ulcer history, recurrent ulceration, one episode of severe hemorrhage, obstruction, perforation, or a large ulcer. Other less common indications that usually indicate

operation are ulceration in an achlorhydric stomach or a positive cytologic smear. Strode[20] has emphasized, in addition, the serious import of any gastric ulceration in the Japanese, since gastric cancer is so common in that race.

In our experience at least half of the patients with gastric ulcer should be subjected to surgery on these indications without delay. The other patients may be handled in a conservative fashion if the patient and physician accept full responsibility for complete cooperation and accurate follow-up studies. Very frequently geographic considerations or the personality of the patient will make surgery advisable. If medical therapy is chosen, the patient usually requires evaluation in the hospital, although protracted treatment and observation may be difficult or impossible because of the expense of hospitalization. Re-evaluation at the end of 10 to 14 days should show diminution in the size of the ulcer if the treatment is to be continued. Repeated examinations are necessary to assure complete healing and absence of recurrent ulceration. Healing should be complete in 4 to 6 weeks, although it may require 8 to 12 weeks in older patients.

CHOICE OF OPERATION FOR GASTRIC ULCER

Insofar as ulcer in the distal stomach is concerned, there is usually little difficulty in selection of the proper operation because there is no competition with partial distal gastrectomy. With ulcers in the fundus, several alternative procedures must be considered. First, however, several operations that have been applied for gastric ulcer merit brief discussion.

Local Excision.—From the historical viewpoint local excision of the ulcer by wedge resection of the stomach should be mentioned first. Many years ago this operation was employed quite frequently as a definitive procedure for chronic gastric ulcer. Recurrence of the ulcer usually followed a year or so later; the ulcer regularly appeared in the same area. Consequently it is not a desirable operation unless the patient is a poor risk and the operation is performed for a major complication of the ulcer. Thus, acute massive hemorrhage from an ulcer near the angle of the stomach in a poor-risk patient may be handled by wedge or sleeve resection. Likewise, when operation is performed for acute perforation of a lesser curvature ulcer, local excision may be carried out to secure an adequate biopsy and satisfactory tissue for closure.

Local excision has also been combined with other procedures, such as distal gastric resection or gastroenterostomy. Distal resection plus local excision of the ulcer has been advocated recently by Denkewalter and Watman[5] for higher gastric ulcers. Not enough patients, however, have been operated upon by such a technique to know whether the mortality will be less or late results different than after high distal gastrectomy.

Gastroenterostomy.—This procedure alone, for years, was the operation of choice in many clinics for gastric ulcer. However, because of the danger of overlooking cancer, gastroenterostomy is regarded universally now as an undesirable method of therapy. Furthermore it has not proved an adequate answer even for benign ulcer, since it did not always lead to healing of the ulcer.

Vagotomy.—Vagotomy with associated procedures such as gastroenterostomy or pyloroplasty that do not include gastric resection were for some time regarded as possible alternatives. A thorough trial of these procedures by many surgeons has convinced even the most ardent advocates of vagotomy that this operation is not indicated for gastric ulcer even if it is assumed to be benign. Dragstedt[6] has emphasized the necessity of removal of the gastric antrum in operations for gastric ulcer on theoretical grounds, since he believes hypersecretion of gastrin by the antral mucosa causes gastric ulcer.

However, one exception may be noted. About 10 per cent of patients with gastric ulcer also have an active duodenal ulcer; here the disease is more typical of duodenal than gastric ulcer, and the measures applicable to duodenal ulcer may be expected to be effective in the treatment of the combined diseases. But, even in this group, a warning should be noted. Although gastric cancer occurs only rarely concomitantly with active duodenal ulcer, it has been observed, and, for that reason, every lesion in the stomach that can be removed with little additional hazard should be excised.

Gastric Resection.—When the ulcer is located at the angulus or in the distal stomach and the stomach is freely movable, it is desirable to carry out a distal resection, removing at least 5 cm. of stomach above the ulcer and continuing distally to excise 3 cm. of duodenum and both omenta. The right gastroepiploic vessels and right and left gastric arteries are ligated near their origins. The corresponding lymphatics are removed. This operation in the light of our present knowledge will provide an adequate procedure for either ulcer or cancer.

A more difficult problem is posed when the ulcer is adherent or has perforated. This occurs not infrequently on the anterior surface of the body of the pancreas. Obviously, if such a lesion were cancer and an en bloc resection considered possible a pancreatoduodenectomy would be necessary. Such an operation on the distal stomach should not be carried out without definite histologic proof that the lesion is cancer, and, even then, we believe, very rarely.

If the lesion apparently is benign, it may be treated by gastric resection, leaving the ulcer base on the pancreas. Any attempt at excision of this base, or cauterization, may lead to a pancreatic fistula. At any rate, drainage of such an area is desirable because pancreatic ducts occasionally are eroded by the ulcer.

Ulcers located proximal to the angulus furnish a much more difficult problem. In nearly all cases it is possible to carry out a distal resection, but the margin of normal stomach above the ulcer will be considerably less than the recommended 5 cm.; it will be adequate if the lesion is a benign ulcer but will leave the surgeon in a somewhat unhappy situation if cancer is present. While the pathologist can furnish a good deal of help at the time of operation, frozen section at this time cannot be depended upon to make the differential diagnosis. In certain institutions this apparently can be done with a high degree of accuracy. In most, including our own, frozen sections are not entirely satisfactory. Consequently, if the surgeon discovers a few days after the

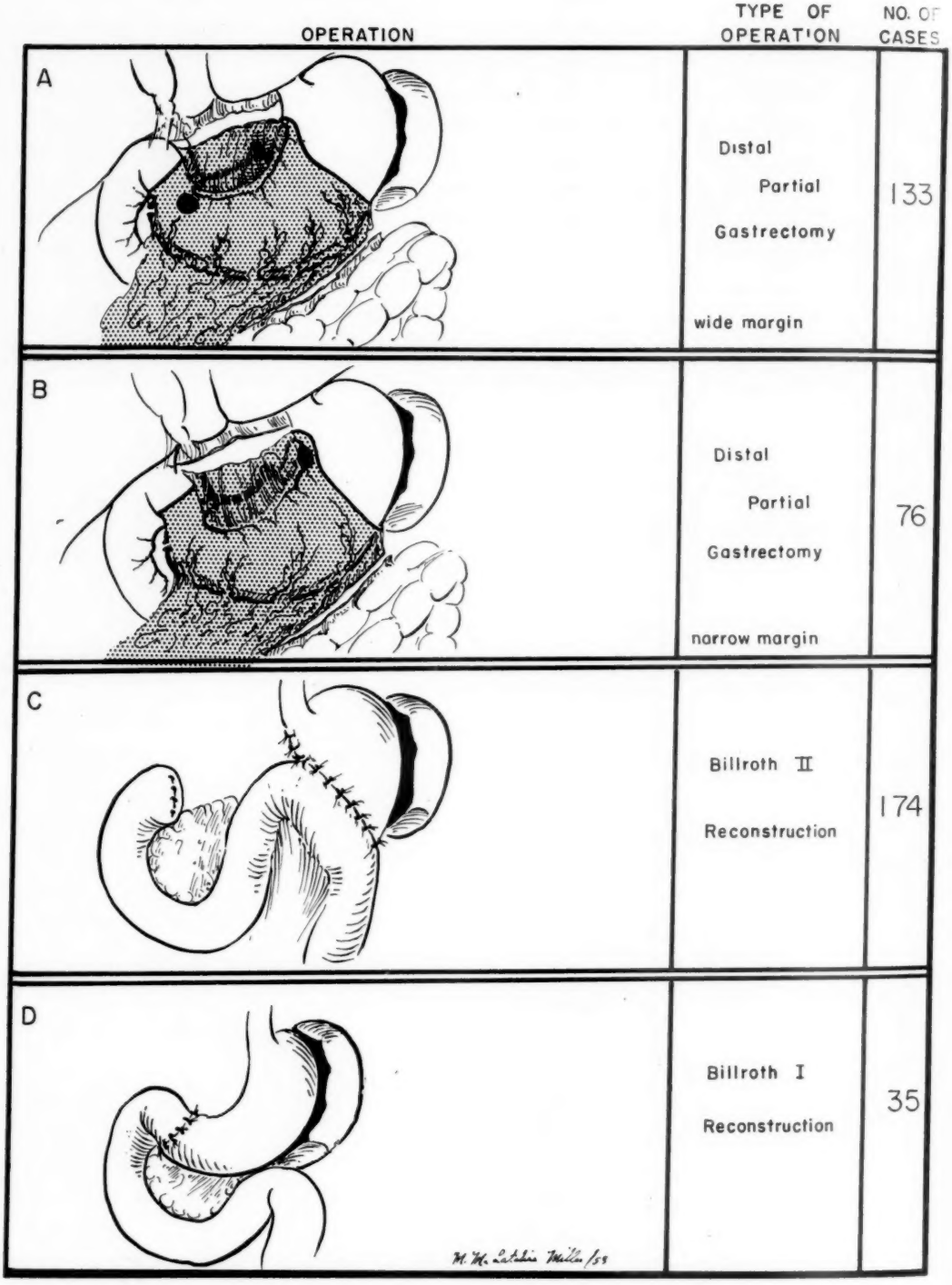

Fig. 1.—*(For legend, see opposite page.)*

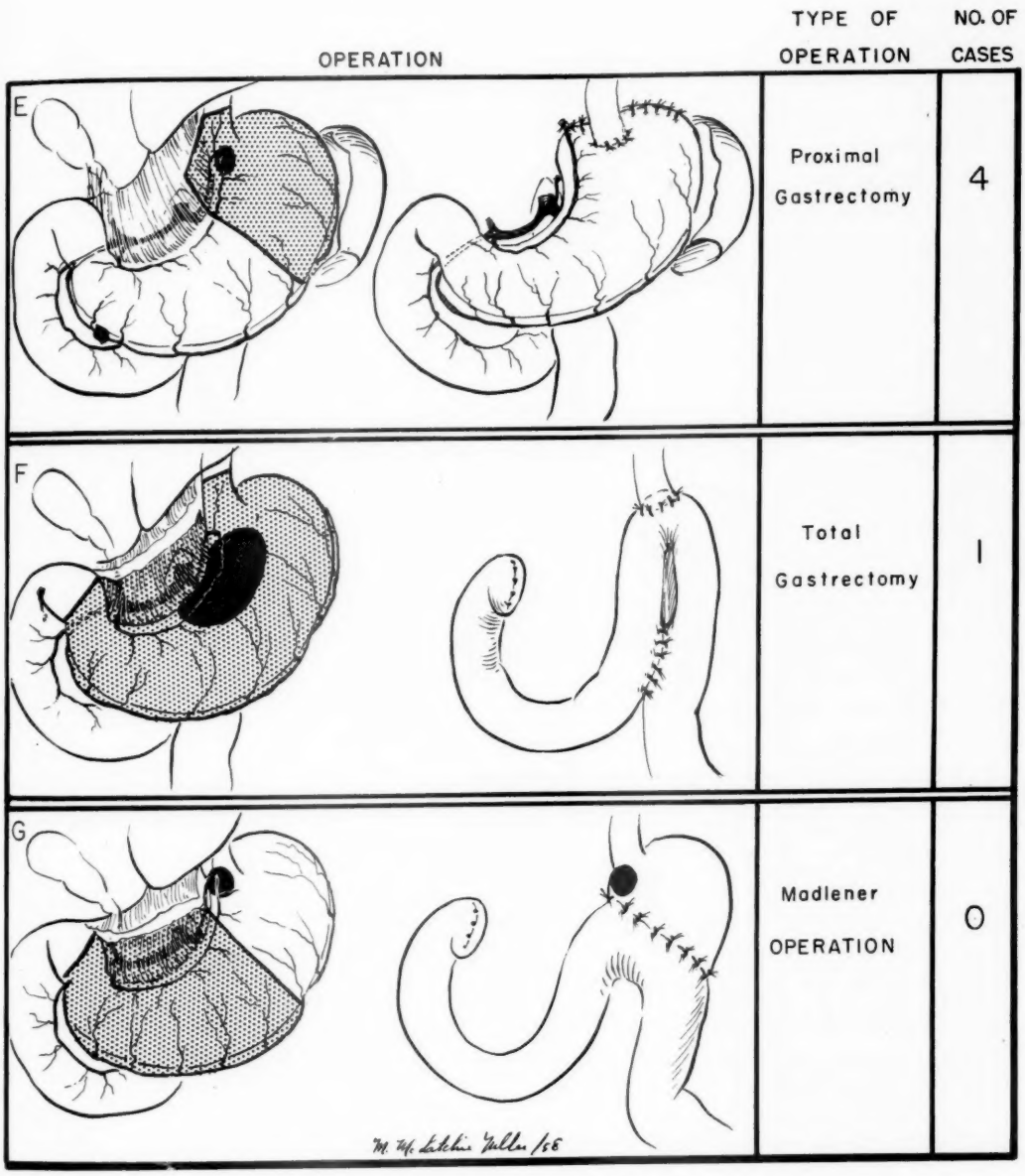

Fig. 1.—Operations for gastric ulcer. *A*, For ulcers in the distal stomach, partial gastrectomy with a wide margin above the lesion is preferred. *B*, For high ulcers, distal gastrectomy with a narrow margin above the lesion is used when the ulcer apparently is benign. *C* and *D*, Gastrointestinal continuity was re-established after operation shown in *A* and *B* by either Billroth I or II methods. *E*, Proximal partial gastrectomy is preferred for juxtaesophageal ulcers. *F*, Total gastrectomy rarely is necessary. *G*, Madlener's operation was not used in this series.

resection that an apparently benign ulcer actually was cancer and if the resection line was involved by cancer and there were no lymph-node metastases, a secondary total gastrectomy is highly desirable.

In this section of the stomach huge ulcers that involve pancreas and spleen sometimes are found. Even if it is known that they are benign they may require total gastrectomy for removal. Here the surgeon will face a difficult decision since a radical operation involving block dissection of stomach, distal pancreas, and spleen may lead to a cure if the lesion is cancer. This extensive procedure is undesirable if the lesion is benign, since partial pancreatectomy introduces the possibility of increased postoperative complications and a total gastrectomy adds to the chances of postoperative gastric crippling.

For this reason, Dragstedt[7] has advised strongly that such an extensive operation should never be carried out without histologic proof that the lesion is cancer. It has been our experience that the lesions which fall into this group fortunately are quite unusual. On the other hand, intragastric biopsy and frozen section diagnosis have not always been easy or eminently successful. Furthermore, the well-known difficulty of obtaining a positive biopsy from a carcinomatous ulcer deserves emphasis. Even permanent sections may be unsatisfactory guides since much of the cancer may have been destroyed by peptic ulceration.

Consequently we believe that resection is the wisest method despite the sequelae of total or partial proximal gastrectomy. It again should be emphasized that these procedures will not often be necessary. Reference to Fig. 1 that demonstrates the type of operation employed in our cases will show that total gastrectomy was required only once and proximal partial gastrectomy four times in the series of 221 operations.

Ulcers at the cardia also may be treated by the Madlener procedure in which the ulcer is left in place and a distal gastric resection is performed. In this country Colp and Druckerman[3] and Gilchrist[8] have used and recommend this method. Our experience with this operation is very small since we believe nearly all gastric ulcers can be treated in some other fashion. However, it might be appropriate to cite data from one of the largest series reported in the literature. Maurer[15] subjected 70 patients to this operation, of whom 3 died. Four ultimately were proved to have cancer in the retained section of the stomach. The 55 patients who apparently had benign ulcer and who were followed did well after operation. It is obvious that, if this operation is selected, the surgeon should biopsy the ulcer at the time of operation and must follow his patients carefully thereafter; if the ulcer is shown by x-ray to increase in size, a secondary resection will be necessary.

The experience of the Mayo Clinic with the high gastric ulcer has been described by Braasch, Cain, and Priestley.[1] In their series, about 5 per cent of all gastric ulcers occur within 2 inches of the esophagogastric junction. Despite the fact that in 21 instances the ulcer was located within 1 cm. of the fundus, partial gastrectomy including the ulcer was possible in 10. In the 6 instances in which the ulcer was immediately adjacent to the esophagus, total gastrectomy was necessary in 4 and esophagogastrectomy in 2. In order of

preference they advise distal gastrectomy including the ulcer, the Madlener procedure, with biopsy of the lesion, and, if there is no other recourse, total or proximal gastrectomy.

After a partial distal gastrectomy the surgeon will have a choice of a Billroth II or I anastomosis. Since many of these patients are elderly, nutrition may be difficult after operation, and a Billroth I anastomosis is desirable when possible. This was done in 35 cases in our series; in one of these an anastomotic ulcer developed requiring a secondary resection. One stomal ulcer also developed in the group which had a Billroth II resection.

FOLLOW-UP STUDIES

Many excellent follow-up studies are available that evaluate the results of treatment of ulcer. They may be considered under several subdivisions as follows: (1) the results of medical therapy of apparently benign ulcer, (2) the results of surgical therapy for benign ulcer, and (3) the results of surgical therapy of the gastric cancer believed preoperatively to be benign ulcer.

1. The Results of Medical Therapy of Apparently Benign Gastric Ulcer.— Attention should be called to two important series of cases that have been reported. In the first, Cain, Jordan, Comfort, and Gray[2] of the Mayo Clinic restricted their study to the apparently benign ulcers that were 2 cm. or less in diameter since these small ulcers were the ones most likely to respond to medical therapy. Complete and permanent healing was possible in only 85 (20.5 per cent) of the 414 patients. Medical management was abandoned for surgical treatment in 33.8 per cent. Cancer was present or developed later in 10.4 per cent of the total group.

It seems reasonable that a closer contact with patients is provided by a clinic that draws patients from a very wide geographic distribution would lead to better results. For example, Smith, Boles, and Jordan[19] studied a group of 1,000 patients who had gastric ulcerations with the appearance of benign peptic ulcer. Four hundred and twenty-two were treated by medical means alone. Of the entire group, 8.8 per cent were proved to have cancer. There were 195 patients who had a satisfactory response to medical therapy who were followed for 5 years or more; 73 per cent of them were without gastric symptoms.

From these series it may be concluded that excellent results may be obtained by medical treatment of approximately 20 to 30 per cent of all patients with apparently benign ulcers while about 10 per cent will prove ultimately to have cancer. The advocates of medical therapy may raise objection that many patients with less serious ulcers are cured before they are referred to one of the large clinics, so that these two series are weighted heavily by intractable ulcers. On the other hand, many patients with hemorrhage from gastric ulcer do not survive to be transported to these clinics. We believe that these arguments essentially balance each other and that it is fair to conclude that about one-quarter of all patients with gastric ulcer will do well on medical therapy.

2. The Results of Surgical Therapy of Apparently Benign Gastric Ulcer.— These results will vary depending upon many factors, including the size of the ulcer, location of the ulcer, and type of the operation employed.

a. The size of the ulcer: The size of the ulcer is comparable roughly to its virulence or lack of amenability to treatment. There is a marked difference between the type of treatment that can be accorded the small and the large gastric ulcer, as shown by the data of Turner and associates.[22] Treatment by resection was followed by a mortality of 1.5 per cent for the small ulcer and 7 for the large (these were over 4 cm. in diameter). Partial gastrectomy was possible in nearly all of the first group, while in many instances total gastrectomy was necessary in the latter.

After operation for the ulcer under 4 cm. in diameter, results according to Comfort and co-workers[4] were satisfactory in 86.7 per cent, fairly satisfactory in 7.4 (in these dumping was a daily problem, even though the patient was happy over his exchange of ulcer symptoms for dumping), and poor in 5.9 per cent (due to postoperative deaths in 1.5 per cent, recurrent or anastomotic ulcer in 2.4, and disabling dumping in 1.6).

b. Location of the ulcer: Ulcers in the distal stomach are easier to diagnose, more accessible, and amenable to less radical operations than those located in the proximal stomach. It therefore should be expected that the results should be better after operation for the distal ulcers.

Distal ulcers are so much more common that any series of statistics on postoperative results of all gastric ulcers essentially represents distal ulcers. As an example, in one of the most optimistic reports available, Marshall and Welch,[14] found that of 105 patients treated by gastrectomy, only one patient had gastric distress thereafter. Insofar as the juxtaesophageal ulcer is concerned, Braasch, Cain, and Priestley[1] followed 44 patients who had such ulcers treated surgically. Twenty-five received a subtotal resection including excision of the ulcer; 17 had excellent results and only 1 had a poor result. There were no recurrent ulcers. Six had total gastrectomy; 3 died postoperatively, and the others had recurrent postresectional difficulties. Two with local resection of the ulcer and gastroenterostomy did poorly, and 2 with partial proximal gastrectomy did poorly. Two with local excision of the ulcer and distal gastric resection did well.

c. Type of operation: There are some conclusions that seem justifiable in the light of the reports quoted previously and of our own experience. Total gastrectomy is poorly tolerated by the patients with benign disease; about one-third of them postoperatively may be expected to have severe limitations and some incapacitating degree of gastric crippling. High distal gastrectomy (approximately 80 per cent) leads to a greater loss of weight than the lower resections; for gastric ulcer, while it is desirable to remove the entire antrum, it is not necessary to remove as much fundus as it is for a duodenal ulcer. Consequently a two-thirds is preferred to a three-quarters resection. A Billroth I reconstruction is preferable to a Billroth II unless there are combined gastric and duodenal ulcers when the resection should be higher and a Billroth II done. The symptoms of dumping, although usually not severe, may occur after any type of operation.

Partial proximal gastrectomy has been employed in the Massachusetts General Hospital for 15 juxtaesophageal ulcers. In an evaluation of this operation, Sweet[21] in 1955 found that the postoperative results in 11 cases done at that time were excellent in the 10 who survived operation. This operation, however, should be combined with a pyloroplasty or gastroenterostomy, since the concomitant bilateral vagotomy may lead to gastric stasis and to recurrent gastric ulcer as noted by Smith, Moulder, and Adams.[18] It must be admitted that other institutions have not been so favorably impressed with proximal gastrectomy; some of these poor results may be due to unrelieved gastric stasis.

3. The Results of Surgical Therapy of Gastric Cancer, Believed Preoperatively to Be Benign Ulcer.—The 5-year survival rate after operation was twice that of the usual cancer of the stomach in cases studied in the Massachusetts General Hospital in 1941, while in the period from 1947 to 1953, of 10 patients with ulcer-cancer, 5 survived 5 years. Hoerr[9] has reported 5-year survivals in 60 per cent. In the largest series available, 33 of 55 patients (60 per cent) from the Mayo Clinic with ulcer-cancer lived 5 years. All studies, therefore, have indicated that the gastric cancer which mimics ulcer is a type that is particularly favorable for cure.

SUMMARY AND CONCLUSIONS

1. The justification of surgical therapy for gastric ulcer resides in the facts that only 20 to 30 per cent of benign ulcers do well on medical therapy and that between 5 and 10 per cent of apparently benign ulcers are actually cancer. On the other hand, after gastric resection, approximately 85 per cent of the patients have good results, compared with 6 per cent who have poor results.

2. The indications for early operation include a long ulcer history, recurrent ulceration, an episode of severe hemorrhage, obstruction or perforation, a large ulcer, ulceration in an achlorhydric stomach, or a positive cytologic smear in the presence of a gastric ulcer.

3. Conflicting reports on the relative frequency of the confusion of gastric ulcer with cancer probably arise from a different selection of cases from which data are derived.

4. Of 367 patients with apparently benign gastric ulcers seen in the Massachusetts General Hospital during the years 1952 through 1957, operation was carried out in 321 (60.2 per cent) with a mortality of 3.6 per cent. The postoperative mortality in 47 patients with acute massive hemorrhage or severe grades of anemia was 10.6 per cent, and in the 174 without hemorrhage, 1.7 per cent. Of these patients, 16 had cancer (7.2 per cent). One hundred and forty-six patients had no operation; 2 are known to have died of cancer later.

5. In the selection of the type of operation there usually is no reasonable alternative to gastric resection. Nearly all ulcers may be treated by some form of distal gastrectomy.

6. If, at the time of gastric resection, an ulcer apparently is benign, both to the surgeon and pathologist, a cancer operation is desirable when the ulcer is distal to the angulus. When the ulcer is higher, the margin of normal stomach proximal to the ulcer may be less since the danger of cancer is counter-balanced by the undesirability of very high or total gastric resection.

7. For the few juxtaesophageal ulcers in which distal gastrectomy is impossible, partial proximal gastrectomy is preferred to the Madlener procedure in the Massachusetts General Hospital.

REFERENCES

1. Braasch, J. W., Cain, J. C., and Priestley, J. T.: Juxta-Esophageal Gastric Ulcer, Surg., Gynec. & Obst. **101**: 280, 1955.
2. Cain, J. C., Jordan, G. L., Jr., Comfort, M. W., and Gray, H. K.: Medically Treated Small Gastric Ulcer; Five-Year Follow-Up Study of Four Hundred Fourteen Patients, J. A. M. A. **150**: 781, 1952.
3. Colp, R., and Druckerman, L. J.: Palliative Gastrectomy in Selected Cases of Gastric Ulcer, Ann. Surg. **124**: 675, 1946.
4. Comfort, M. W., Priestley, J. T., Dockerty, M. B., Weber, H. M., Gage, R. P., Solis, J., and Epperson, D. P.: The Small Benign and Malignant Gastric Lesion, Surg., Gynec. & Obst. **105**: 435, 1957.
5. Denkewalter, F. R., and Watman, R. N.: Conservative Surgical Treatment of All Gastric Ulcers, A. M. A. Arch. Surg. **75**: 558, 1957.
6. Dragstedt, L. R.: A Concept of the Etiology of Gastric and Duodenal Ulcer, Caldwell Lecture, 1955, Am. J. Roentgenol. **75**: 219, 1956.
7. Dragstedt, L. R.: Personal communication.
8. Gilchrist, R. K.: Surgical Treatment of High-Lying Gastric Ulcer, J. A. M. A. **162**: 1039, 1956.
9. Hoerr, N. L.: Personal communication.
10. Holmes, G. W., and Hampton, A. O.: Incidence of Carcinoma in Certain Ulcerating Lesions of Stomach, J. A. M. A. **99**: 905, 1932.
11. Lahey, F. H.: In discussion of Ransom, H. K.: Subtotal Gastrectomy for Gastric Ulcer; a Study of End Results, Ann. Surg. **126**: 633, 1947.
12. Lampert, E. G., Waugh, J. M., and Dockerty, M. B.: The Incidence of Malignancy in Gastric Ulcers Believed Preoperatively to Be Benign, Surg., Gynec. & Obst. **91**: 673, 1950.
13. Mallory, T. B.: Carcinoma In Situ of Stomach and Its Bearing on Histogenesis of Malignant Ulcers, Arch. Path. **30**: 348, 1940.
14. Marshall, S. F., and Welch, M. L.: Results of Surgical Treatment for Gastric Ulcer, J. A. M. A. **136**: 748, 1948.
15. Maurer, H.: Die Operation nach Madlener und ihre Ergebnisse, Beitr. klin. Chir. **182**: 266, 1951.
16. Ochsner, A.: Personal communication.
17. Ravdin, I. S.: Quoted in reference of Strode, J. E.: Surg. Gynec. & Obst. **98**: 607, 1954.
18. Smith, C. A., Moulder, P. F., and Adams, W. E.: Gastric Ulcer Following Esophagogastric Anastomosis for Carcinoma of the Esophagus or Gastric Cardia, Ann. Surg. **146**: 630, 1957.
19. Smith, F. H., Boles, R. S., Jr., and Jordan, S. M.: Problem of the Gastric Ulcer Reviewed. Study of One Thousand Cases, J. A. M. A. **153**: 1505, 1953.
20. Strode, J. E.: In Support of Surgical Removal of Small Ulcerating Lesions of the Stomach Without Benefit of Medical Treatment, Surg. Gynec. & Obst. **98**: 607, 1954.
21. Sweet, R. H.: Personal communication.
22. Turner, J. C., Jr., Dockerty, M. B., Priestley, J. T., and Comfort, M. W.: A Clinicopathologic Study of Large Benign Gastric Ulcers, Surg., Gynec. & Obst. **104**: 746, 1957.
23. Welch, C. E.: The Treatment of Upper Gastro-intestinal Hemorrhage, Am. Surgeon **23**: 900, 1957.
24. Welch, C. E., and Allen, A. W.: Gastric Ulcer: The Significance of This Diagnosis and Its Relationship to Cancer, Ann. Surg. **114**: 498, 1941.
25. Welch, C. E., and Allen, A. W.: Gastric Ulcer. A Study of the Massachusetts General Hospital Cases During the Ten-Year Period, 1938-1947, New England J. Med. **240**: 276, 1949.
26. Welch, C. E., and Wilkins, E. W., Jr.: Carcinoma of the Stomach, Ann. Surg. In press.

Editorial

CONDUCTED BY I. S. RAVDIN, M.D.

A Rebuttal to "Hemorrhoidectomy—Need for a Sound Reappraisal"

The reason for writing this rebuttal to Dr. Lewis's editorial (SURGERY **44**: 431, 1958) is my disagreement with a number of points raised by him and particularly "that a conscientious physician cannot find enough information either in the medical literature or in the local hospital to make a sound appraisal of the operation." In the interest of clarity and brevity, I will reply mostly with quotations taken from my own recent papers in full realization that it is not always safe to quote statements out of context.

My reply to the statement that "there seems to be no *attempt* to study the results of the operation or to compare the effectiveness of operative treatment with nonoperative treatment of the disease" is as follows:

1. The management of hemorrhoids offers three alternatives: They may be neglected, injected, or resected. (Problems in Hemorrhoidal Disease, Editorial, Surg., Gynec. & Obst. **103**: 115, 1956.)

2. In spite of a voluminous literature the merits and demerits of injectional sclerosing and surgical therapies are still poorly understood by most of the profession. This is largely the result of overemphasis on injectional therapy by those incapable of performing surgical procedures and overemphasis on the operative approach by surgeons who are unacquainted with the conservative methods of treatment. In recent years, however, it has become apparent that anyone treating hemorrhoids should be capable of performing both forms of therapy. (Proctology and the General Practitioner, New York J. Med. **52**: 1009, 1952.)

3. To complete this investigation, I felt it desirable to compare and contrast surgical excision with injectional therapy. After treating 6 patients by operation for internal hemorrhoids that I regarded as suitable for injectional therapy, I became so convinced that small and moderate-sized internal bleeding hemorrhoids do not warrant an operative procedure that I discontinued the clinical experiment. However, renewed and ample opportunity to compare and contrast the two procedures was afforded to me while serving in the Army, as soldiers with symptomatic internal hemorrhoids (which in civil practice are considered suitable for injectional therapy) are treated by operation. This added observation and experience confirmed the conclusions of the study of the experimental series of cases in civilian practice, namely,

that the majority of cases of symptomatic small or moderate-sized internal hemorrhoids do neither warrant nor require hemorrhoidectomy with the attendant remote, but potential, risk incident to an anesthetic and a surgical procedure, and the loss of work or duty hours. This is especially true when most, if not all, of these patients can be satisfactorily treated by the ambulatory injectional method. (Injectional Treatment of Internal Hemorrhoids, Am. J. M. Sc. **213**: 350, 1947.)

4. A study of 67 such patients with systemic disease on whom I have eventually performed hemorrhoidectomies following unsuccessful injectional sclerosing therapy has convinced me (as well as the patients) of the superiority of surgery where clear-cut local indications for hemorrhoidectomy exist. This conclusion was reinforced after treating by injection a *still larger number* of intelligent patients with mixed piles who, *for business reasons,* were unable to undergo hemorrhoidectomies at the time of their initial consultation. All of these patients expressed their preference for the operation. (Adenomas and Hemorrhoids: Problems of Rectal Bleeding, Wisconsin M. J. **54**: 413, 1955.)

Patients who have either large internal or internoexternal (mixed) hemorrhoids with pain, protrusion, or bleeding require surgical intervention and are but temporarily helped when treated "by conservative methods alone" including "*some* good advice about personal hygiene and perhaps a few days of bed rest." I am yet to be shown that "careful soap and water cleansing of the anus after each bowel movement, or at least once a day, is effective in clearing the chronic infection that is generally recognized as the usual cause of painful hemorrhoids."

Is chronic infection really the cause of hemorrhoids or of "painful hemorrhoids"? Although I had at one time accepted this factor as at least one of the important causes, I now doubt this because:

Hemorrhoidal tissue removed at operation and that obtained from rectums extirpated for cancer, as well as that removed at necropsy in subjects with nonintestinal disease, invariably show the same histologic picture, namely, dilated veins with variable degrees of inflammatory reaction but without evidence of infection. (Present Status and Modern Treatment of Hemorrhoids, New York J. Med. **56**: 2245, 1956.)

Futhermore, are pathologists of "no help" in this regard? Note this clear-cut histologic report: "The hemorrhoidal vessels are large, numerous and lie very superficially beneath the epithelium. None appears thrombosed. Inflammatory reaction is absent." (Adm. No. 57-8349.)

The question "is it possible that the painstaking care given to these patients after hemorrhoidectomy in order to obtain a rapid convalescence would cure most of them even without an operative procedure" has already been partially answered. This question brings up another important facet, namely, is this painstaking postoperative care necessary?

1. My recent studies have disclosed that the conventional periodic digital explorations or examinations, or the special topical application of medications such as vitamins, chlorophyll, and so forth, to anorectal wounds following the open technique of hemorrhoidectomy failed to influence or expedite the healing process of the wounds; the controls

in whom the postoperative wounds were left practically undisturbed healed just as effectively. These maneuvers are performed regularly either as a result of custom, habit, and tradition, or their use is dictated by the dire need resulting from a poorly conceived new technique or a poorly executed initial orthodox hemorrhoidectomy.'' (Problems in Hemorrhoidal Disease, Editorial, Surg., Gynec. & Obst. **103**: 115, 1956; Healing of Anorectal Wounds With Reference to ''Rectal Medication,'' A. M. A. Arch. Surg. **73**: 870, 1956.)

2. Therapeutic crutches in the form of frequent digital or instrumental anal dilations and drugs are no substitutes for basic concepts and sound surgical principles. The surgical treatment of lesions of the sensitive anorectum, like any other type of operation, should be based on the solid principles of surgery laid down by Halsted. (Healing of Anorectal Wounds, Editorial, J. A. M. A. **166**: 780, 1958.)

Surgeons of experience know that the healing of surgical wounds anywhere in the body may be delayed but cannot be expedited because under normal conditions natural healing proceeds at a maximum rate.

As I see the problem, ''the crucial question'' is *not* only ''whether the operation is being done for good reasons'' but also whether the chosen technique is well performed. Also, the large number of techniques of hemorrhoidectomy (most of which are based on the principles first enunciated by Hippocrates) described in the literature at once indicates dissatisfaction with the operation by many surgeons. I believe that most surgeons will resent the statement that ''any surgeon not manifesting a primary interest in proctology who does a large number of hemorrhoidectomies is a fair target of criticism.'' A good many of the posthemorrhoidectomy complications that I see in consultation (my own probably gravitate to other surgeons) have originated in the hands of the ''specialists'' so why spank the ''occasional'' and, by implication, the general surgeon.

Although I am in disagreement with Dr. Lewis on many issues I congratulate him for raising the various questions in print thus making a debate possible in the true American way.

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Calendar of Surgical Meetings

AMERICAN ACADEMY OF NEUROLOGICAL SURGERY. *Annual Meeting,* Nov. 5-8, 1958, Royal York Hotel, Toronto, Ontario, Canada. Secretary, Dr. Robert McLaurin, University of Cincinnati, Cincinnati, Ohio.

AMERICAN COLLEGE OF SURGEONS. *Southern California Chapter,* Jan. 16-18, 1959, Coronado Hotel, San Diego, Calif. Secretary-Treasurer, Dr. Max R. Gaspar, 211 Cherry Ave., Long Beach 2, Calif.

AMERICAN MEDICAL ASSOCIATION. *Annual Meeting,* Dec. 2-5, 1958, Leamington Hotel, Minneapolis, Minn. Deadline for submission of abstracts, Aug. 1, 1958. Secretary, Council on Scientific Assembly, Dr. Thomas G. Hull, 535 North Dearborn St., Chicago 10, Ill.

SOCIETY OF UNIVERSITY SURGEONS. *Annual Meeting,* Feb. 12-14, 1959, Denver, Colo. Secretary, Dr. James D. Hardy, University of Mississippi Medical Center, Jackson, Miss.

SOUTHERN SURGICAL ASSOCIATION. *Annual Meeting,* Dec. 9-11, 1958, Boca Raton Hotel and Club, Boca Raton, Fla. Attendance by invitation of membership only. Secretary, Dr. George G. Finney, 2947 St. Paul St., Baltimore 18, Md.

WESTERN SURGICAL ASSOCIATION. *Annual Meeting,* Nov. 20-22, 1958, Hotel Kahler, Rochester, Minn. Deadline for submission of papers, Sept. 1, 1958. Secretary, John T. Reynolds, M.D., 612 N. Michigan Ave., Chicago 11, Ill.